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ENDEMIC ROCKY MOUNTAIN SPOTTED FEVER IN MASSACHUSETTS

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BOSTON AND HYANNIS, MASSACHUSETTS

ALTHOUGH Rocky Mountain spotted fever has been reported from all geographical regions in the United States,[1] it was not recognized in New England prior to 1937, when 2 cases were discovered in Rhode Island[2] and 1 in Massachusetts.[3] From that time until 1942 at the end of the so-called "tick season" 8 cases were reported from four of the six New England states: Massachusetts, 4; Rhode Island, 2; Connecticut, 1; and New Hampshire, 1. The source of infection of 3 of these cases was found to be in regions outside of New England. The 5 remaining cases originated in Massachusetts, which is apparently the sole New England state where the disease is endemic.

All 5 Massachusetts infections were acquired on Cape Cod. Four cases were attributed to three contiguous communities comprising an area of fifty-nine square miles. It must be borne in mind that all endemic Massachusetts cases occurred during the three-year interval from 1937 to 1939, and that this disease has not reappeared on Cape Cod since 1939.

The distribution according to the month of onset of the Massachusetts cases was as follows: May, 1; June, 1; July, 3. The dog tick, *Dermacentor variabilis*, which is the vector of this disease in the East, becomes most plentiful during the latter part of May or early in June, and declines sharply after mid-July.[4] There is usually a lag of several weeks between the time of maximum abundance of ticks and the peak in case incidence.[5]

Of the 5 cases endemic in Massachusetts, 3 have been reported previously.[2, 3] This paper will include a discussion of the two remaining cases. From one of these the causative virus was recovered[6] and has been maintained by serial passage in guinea pigs. The isolation of this virus has presented the only opportunity to study the endemic agent responsible for Rocky Mountain spotted fever in Massachusetts.

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CASE REPORTS

CASE 1.‡ R. E., a 4-year-old boy, was admitted to the Children's Hospital on June 5, 1939, with complaints of difficulty in walking and fever of 1 week's duration. He came from Cape Cod, where he had been bitten by several ticks during the 3 weeks before admission. He had been well until 1 month before admission, when he developed a limp for which a local physician could find no explanation. Nine days before entry, he became irritable and the temperature was found to be elevated. He complained of severe headache and joint pains so severe that he was unable to stand. Two days later a rash appeared, beginning on the wrists and ankles and spreading to the trunk, neck and face. The temperature remained elevated throughout the week before admission.

On admission the temperature was 101.2°F., the pulse 100, and the respirations 20. There was moderate generalized adenopathy. Although limitation of motion was noted in the shoulders, wrists, fingers and ankles, no outward changes could be detected. There was a generalized maculopapular eruption (Figs. 1 and 2). The lesions were discrete and measured from 2 to 3 mm. in diameter; they were present on the head, neck, trunk and extremities, including the palms and soles. The remainder of the physical examination revealed no other abnormality.

Urinalysis was essentially negative. The red-cell count was 3,600,000, and the hemoglobin 90 per cent (Sahli). The white-cell counts ranged from 20,000 on admission to 8600 on June 14. Blood smears were normal. Lumbar puncture on June 6 showed no abnormal findings. Tuberculin tests on June 6 and June 8 were negative. A blood culture taken on June 5 was negative. A blood Hinton test on June 5 was negative. A Weil–Felix reaction on June 5 was positive in a dilution of 1:5120. Electrocardiograms on June 7 and 14 were not remarkable. Chest plates on June 5 and 7 showed slight peribronchial congestion.

The patient was drowsy and apathetic during the first 2 days. The temperature remained elevated during this time and became normal on the 3rd hospital day, al-

‡We are indebted to Drs. Richard M. Smith and John A. V. Davie of the Children's Hospital for permission to publish this case report.

though it rose to just above 100°F. on one or two occasions thereafter. The pulse averaged 120 for several days. The rash gradually disappeared and had faded completely at the end of a week. Recovery was uneventful, and the joint complaints had disappeared completely at the time of discharge.

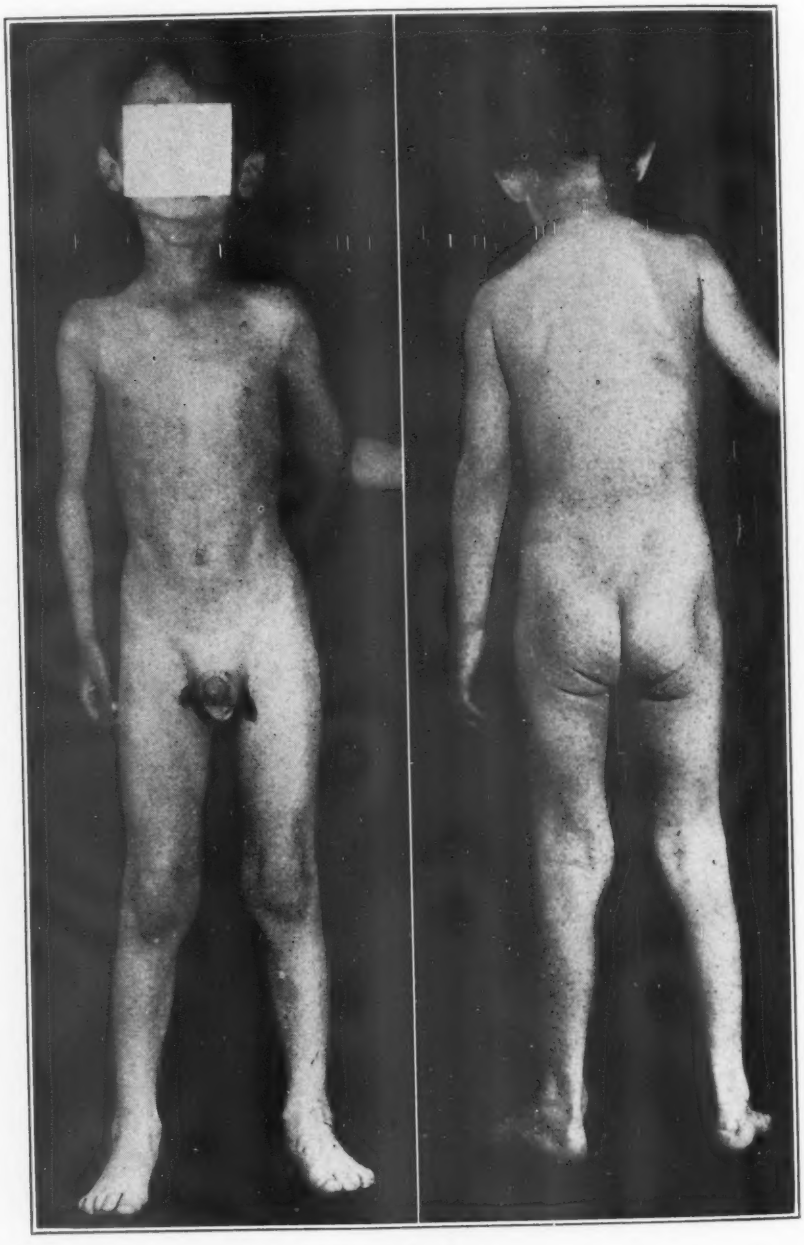

FIGURE 1. *Case 1.*
The photographs show the generalized maculopapular eruption.

CASE 2. M. E. S., an 8-year-old girl residing in Dennis, Massachusetts, was admitted to the Cape Cod Hospital in Hyannis on June 12, 1938, with complaints of headache, fever and malaise. She had been well until 5 days previous to admission, when she began to complain of severe frontal headache, which persisted for several days. There was gradually increasing restlessness, irritability and a whimpering cry at night. On the 4th day of the illness, a macular eruption appeared on the buttocks and spread to the arms, legs and face. The temperature during the first 5 days of the illness varied between 99 and 105°F. At times the patient was irrational. The past history was not contributory; there had been the usual childhood diseases. Seven siblings and the parents were living and well.

On admission the temperature was 100.8°F., and the pulse 120. Physical examination revealed a well-nourished

child lying apathetically in bed. The face was dusky. Except for an eruption on the skin, the examination was negative. Maculopapular lesions were generally distributed over the face, forearms, both buttocks and the labia majora. These lesions were discrete in some areas and confluent in others, and faded on pressure.

FIGURE 2. *Case 1.*
This photograph shows the eruption on the soles of the feet.

Urinalysis showed varying degrees of albuminuria from June 12 to July 12. The red-cell count, which was 4,500,000 on admission, gradually dropped to 2,600,000 on July 6. Hemoglobin determinations ranged from normal levels at admission to 45 per cent (Sahli) early in July. The white-cell count rose from 7200 on June 12 to 23,000 on June 16. During the subsequent months it fell slowly to about 12,800. Differential counts were not unusual except for a moderate increase in polymorphonuclear leukocytes to about 85 per cent during the first 10 days of the illness. A blood culture taken on June 21 was negative. A lumbar puncture on August 1 revealed a clear fluid, no increase in pressure and a total cell count of 34 lymphocytes. The blood chemical findings were normal. A lumbar puncture on September 2 showed no abnormalities. Electrocardiograms were reported as follows: June 26, PR interval of 0.16 second; July 26, sinoauricular tachycardia and a PR interval of 0.20 second; October 12, PR interval of 0.16 second and a high takeoff of the ST interval in Leads 1 and 2. The serologic studies* were as follows: the Weil–Felix reaction was positive in dilutions of 1:320 on June 15, of 1:640 on June 22 and of 1:320 on July 4; on June 22, the agglutination reaction with a rickettsial antigen was positive in a dilution of 1:640; and on February 15, 1943, a complement-fixation test for Rocky Mountain spotted fever was positive in a dilution of 1:128 and one for endemic typhus was negative. On June 15, 1938, 3 cc. of blood was inoculated at the bedside into two guinea pigs. The infectious agent was isolated from each animal.

The rash noted on admission gradually faded and was replaced on the 8th day of the illness by a generalized petechial eruption somewhat accentuated on the wrists, ankles and upper back. There were few lesions on the face and the anterior aspect of the trunk. On June 17, a nonpitting edema was noted on the face, eyelids and feet. The rash, which had been bright pink, assumed a darker hue. In some areas where the eruption appeared to be most hemorrhagic the lesions coalesced to form large purplish blotches. These were most prominent over the wrists and feet. Three days later the rash became more extensive as a fresh crop of petechiae appeared.

The irritability noted on admission persisted. Although stuporous at times, the patient could be aroused to respond to questions. She gradually lapsed into coma. There was evidence of increasing involvement of the central nervous system. The pupils became dilated and did not react to light. There was slight weakness of the left side of the face. Control of the vesical and anal sphincters was lost. From day to day there was considerable variation in the neurological signs. Having lost the ability to take food by mouth, the patient was fed by gavage, and this had to be continued until October 16. She remained comatose for about 3 months. During this period no voluntary muscular movements could be detected. On August 6, the patient began having numerous attacks of opisthotonos lasting from a few minutes to several hours. These attacks recurred for 3 weeks. During the latter part of September movements of the fingers and arms were first noted. Feeding by stomach tube was discontinued as the swallowing reflexes were restored. Mental recovery was slow. On October 27, the patient spoke for the first time in 4 months. At discharge on December 7, she was alert mentally, although she still spoke in a whisper.

Beginning June 22, extensive sloughing of the skin was noted. This continued until a considerable proportion of the body integument was involved, including the skin of the left leg, left midthigh, both knees and the extensor surface of the upper and lower thirds of the right thigh. These areas healed quite slowly and were eventually the sites of extensive scar-tissue formation.

On July 29, the course was further complicated by intermittent attacks of acute pulmonary edema. During these episodes the pulse became rapid, and auscultation revealed coarse rales throughout both lung fields.

During the early part of the illness the temperature and pulse were markedly elevated, the temperature on June 24 having been recorded as 106°F. (axillary). Fever of considerable degree persisted until late in September, a period of 3 months. From October to November it varied from 98 to 101°F. and it gradually became normal late in November. The pulse level corresponded in general with that of the temperature. The total duration of elevated temperature was 5½ months.

Shortly after discharge, the patient was able to stand alone for the first time in several months. As mental improvement continued, she was soon able to read and write. She was readmitted in August, 1939, because of difficulty in walking owing to contracting scar tissue in the region of the sacrum and both thighs. There was marked

*The agglutination tests were performed by Florence K. Fitzpatrick, Ph.D., of Sharp and Dohme, Incorporated, Glenolden, Pennsylvania, and the complement-fixation tests by Dr. I. A. Bengtson, of the United States Public Health Service.

relief following plastic surgery of the skin. In 1942, the patient's mentality had been completely restored.

Bacteriologic data. The infectious agent was recovered by intraperitoneal inoculation of guinea pigs with blood from the patient taken on the 8th day of the illness. In subsequent studies, the incubation period of the disease in the guinea pig was about 5 days.[6] The agent was apparently not exceedingly virulent for guinea pigs, since there were no fatalities among any of the inoculated animals. Although all the guinea pigs reacted to the injection of the agent by showing elevation of temperature, only 30 per cent of them showed noticeable scrotal swelling. All the animals that recovered were found to be solidly immune when reinoculated with a virulent strain of Rocky Mountain spotted fever. The isolated agent was effectively neutralized by convalescent serum obtained from the patient. Animals already immune to Rocky Mountain spotted fever did not react to inoculation with the agent.

Convalescent serum obtained 4½ years after onset of the disease in 0.5-cc. and 0.25-cc. amounts neutralized completely a Bitter Root Valley strain of Rocky Mountain spotted fever virus.[7] Control animals receiving the same virus together with normal human serum died of the disease.

Discussion

Since 1931, when the identification of Rocky Mountain spotted fever in the eastern part of the United States[8] led to the discovery of numerous cases in that region, it had been held that this disease was more fatal in the West than in the East. Laboratory data supported this idea for several years. Strains isolated in the West were more virulent for guinea pigs than were those recovered in the East. During 1940, however, Topping and Dyer[9] were successful in isolating from a patient in Washington, D. C., a highly virulent strain of Rocky Mountain spotted fever virus that had many characteristics of the most virulent strains obtained from Bitter Root Valley, Montana. According to the reactions of this virus in guinea pigs,—that is, the duration of the incubation period, the ability to produce fatal disease, and the scrotal lesions,—the Washington strain was highly virulent. Furthermore, in 1941 a strain of low virulence was recovered from a case in Wyoming.[10] Statistical studies had already shown that when fatality rates of Eastern and Western cases were arranged according to comparable age groups, apparent differences between them vanished.[11] Hence, the terms "Eastern" and "Western" when applied to Rocky Mountain spotted fever had lost their former significance.

The strain isolated in Massachusetts, when judged by the usual criteria, was of low virulence. However, the clinical course of the patient from whom the virus was isolated was by no means mild. Actually this case presented clinical findings ordinarily associated with the severest type of infection. Marked involvement of the central nervous system with coma, opisthotonos, muscle tremors and severe cutaneous manifestations, such as a confluent hemorrhagic eruption followed by necrosis and sloughing, is found in most fulminating cases.[12] The patient in Case 2 showed all these findings. Moreover, the prolonged hyperpyrexia and severe mental disturbance offer additional evidence of an exceedingly severe infection.

Rumreich, Dyer, and Badger[13] in 1931 observed that disturbances of the central nervous system in Rocky Mountain spotted fever are often severe. Wolbach,[14] discussing the pathology of this disease, described focal brain lesions often associated with thrombosis of small blood vessels and necrosis. Hassin[15] described a fatal case in an eleven-year-old girl who, in addition to coma and a confluent hemorrhagic rash, presented signs of meningeal irritation including rigidity of the neck, a positive Kernig sign and a count of 10 cells in the spinal fluid. The histopathology at post-mortem examination was described as a nonsuppurative meningoencephalitis. Although spinal-fluid findings in cases of Rocky Mountain spotted fever are usually within normal limits, pleocytosis is occasionally noted. Carey[16] in 1939 reported 2 cases with spinal-fluid counts of 24 and 224 cells, respectively; the smear in the second case revealed 12 per cent polymorphonuclear leukocytes and 88 per cent lymphocytes. A third case presented xanthochromic fluid. Apparently central-nervous-system manifestations of Rocky Mountain spotted fever are at times an integral part of the clinical picture.

Patients may exhibit varying degrees of edema. As in Case 2, this occurs during the acute stage of the illness. Parker[17] observed that albuminuria is frequently encountered and that complete urinary retention may occur. Ong and Raffetto[18] analyzed 18 cases in children and noted edema in 4 of them. In 2 cases the edema was generally distributed, and in the other 2 it was local, affecting the hands and feet in one patient and the face and feet in the other. The exact cause of this edema, which is usually nonpitting, has not been established. One might postulate a marked reduction in serum protein as a possible explanation. No studies concerning this aspect of the disease could be discovered in the literature.

The early diagnosis of Rocky Mountain spotted fever depends primarily on the evaluation of the available clinical data. Unfortunately, all serologic tests are negative during the first week of the disease. It was recently stated that the Russians have developed a method by which typhus fever can be diagnosed on the second or third day.[19] No details concerning this test have as yet been revealed. Isolation of the Rocky Mountain spotted fever virus must be performed early in the disease before lysis has occurred. This proce-

dure, however, is lengthy, and there is considerable delay before the etiologic agent is definitely identified. The Weil–Felix reaction, using various strains of the genus Proteus, has been useful in the diagnosis of rickettsial disease after the first week of illness. This test, however, does not distinguish between typhus fever and Rocky Mountain spotted fever. Epstein[20] in 1922 and Zinsser and Castañeda[21] in 1932 showed that convalescent serums agglutinate rickettsial antigens. Fitzpatrick and Hampil[22] observed that in infected rabbits the development of rickettsial agglutinins precedes that of Proteus agglutinins. Recently Bengtson and Topping[23] demonstrated the value of the complement-fixation test in the diagnosis of rickettsial infections. They suggested that this test can be used in the differential diagnosis of Rocky Mountain spotted fever and typhus fever. In cases of typhus fever significant titers are obtained by this test on the ninth and tenth days after onset. The reaction remains positive for many years after recovery. Thus, in Case 2 a positive complement-fixation test for Rocky Mountain spotted fever in a dilution of 1:128 was obtained four and a half years after onset. The complement-fixation test for typhus fever was negative.

The only laboratory confirmation of the diagnosis of Rocky Mountain spotted fever in Case 1 was the Weil–Felix reaction. However, the history of several tick bites, the clinical picture and the positive agglutination reaction leave little doubt concerning the diagnosis.

Recently Topping[24] found that monkeys and guinea pigs survived experimental inoculation with the virus of Rocky Mountain spotted fever following the administration of a hyperimmune rabbit serum. Tissues of infected ticks were used as the antigen in the preparation of this serum. Kurotchkin, von der Scheer and Wyckoff[25] then showed that an effective serum results from injecting rabbits with rickettsiae cultivated in the yolk sac according to the method of Cox.[26] Newer methods used in the cultivation of rickettsiae have facilitated considerably the development of rickettsial vaccines and therapeutic serums.[6, 26, 27] The successful use of serum in the treatment of experimentally infected animals has suggested its application to human cases of Rocky Mountain spotted fever. Such a therapeutic serum is now available commercially.* It is to be expected that this form of treatment should be most effective early in the course of the disease, before the serologic tests become positive. Hence, familiarity with the clinical signs and symptoms of Rocky Mountain spotted fever is important.

A prophylactic vaccine made from the tissues of infected adult wood ticks (*D. andersoni*) has been available for many years.[28] Field studies performed in the West with this killed vaccine have demonstrated that it has definite immunizing value. In 1937, Bengtson[29] reported protection against infectious doses of the Rocky Mountain spotted fever virus in guinea pigs previously immunized by a formalized rickettsial antigen prepared from infected guinea-pig tissues grown in tissue culture. Cox,[30] in 1939, demonstrated the protective value for guinea pigs of vaccine prepared from rickettsiae cultivated in embryonic chick tissue. In Massachusetts the risk of acquiring Rocky Mountain spotted fever, even in the endemic area, is so small that routine prophylactic inoculation is scarcely justifiable.

The possibility of the future occurrence of Rocky Mountain spotted fever in Massachusetts merits careful consideration. At first glance some reassurance may be derived from the failure of any new cases of Massachusetts origin to appear since 1939. In 1935, Parker,[31] however, called attention to the tendency of this disease to occur in cycles. Hence, in some local endemic areas in the West, intervals between cases were sometimes quite prolonged. In one county the disease disappeared for nine consecutive years only to reappear. This phenomenon is particularly likely to occur in regions similar to the endemic area in Massachusetts, where Rocky Mountain spotted fever exists in a localized region.

It is odd that Massachusetts remained free of this disease until 1937. Although the clinical manifestations of Rocky Mountain spotted fever are striking, experience in other states has demonstrated that the disease frequently goes unrecognized.[13] It is now well known that prior to 1931 these cases were often labeled "endemic typhus." Investigation of the records of the Massachusetts Department of Public Health did not, however, bring to light any similar confusion. Observations in the West have shown that the virus of Rocky Mountain spotted fever can exist for many years in the ticks of a given area without the occurrence of the disease in man.[32] Later, owing to some factor as yet unknown, the disease suddenly makes its appearance.

Although thousands of persons are exposed to ticks each spring and summer throughout Cape Cod and its adjoining islands, the paucity of cases of Rocky Mountain spotted fever indicates that the proportion of infected ticks is small. Of the three species of ticks concerned in the natural transmission of the disease, two varieties are present on the Cape; namely, the dog tick (*D. variabilis*) and the rabbit tick (*Haemaphysalis leporis-palustris*). Surveys conducted in 1938 showed that

*Manufactured by the Lederle Laboratories, Incorporated, Pearl River, New York.

although the dog tick is found throughout the New England states, it is most plentiful on Cape Cod and the islands of Martha's Vineyard, Nantucket and Naushon.[4] In the East, only the dog tick causes the transmission of the disease to human beings. The rabbit tick, which does not bite man, is important in the maintenance of the virus in nature and is only indirectly involved in the occurrence of the disease in man.[5]

There are several factors that help to maintain and propagate the virus in nature. Experimental work with *D. andersoni* has demonstrated that the infectious agent, once acquired by the immature forms of the tick, is passed on to the adult stage.[33] The agent is also transmissible through the ova of infected females. Furthermore, when infected immature or adult forms of the tick feed on a susceptible host, this host becomes infected, and other ticks that feed on this host during the infectious stage may acquire the virus.[17] Studies with *D. variabilis* have suggested a similar method of transmission.[34]

It might be argued that the endemicity of Rocky Mountain spotted fever in Massachusetts is a temporary and perhaps accidental occurrence rather than a natural phenomenon, and that the virus was brought into this area by infected ticks on dogs, these ticks in turn transmitting the virus to native Massachusetts ticks. Another possible avenue of introduction is by means of the rabbit tick. For many years rabbits have been imported into the Cape for hunting purposes. Parker[35] has postulated that in the West the virus of Rocky Mountain spotted fever passes from infected rabbit ticks to previously uninfected wood ticks through the rabbit, a host common to both species. Although the adult dog tick is rarely found on the rabbit, the accession catalogue of the United States Bureau of Entomology and Plant Quarantine, reveals that the immature forms are more frequent on the rabbit.[4] A similar mechanism may be assumed in the East. On the other hand, the simultaneous appearance of Rocky Mountain spotted fever throughout widespread areas in the East suggests long-standing endemicity rather than a gradual spread from one region to another. Nevertheless, the situation in Massachusetts, where relatively few cases have been discovered, may not be entirely analogous to that in other Eastern areas where the disease is more prevalent. No matter how the virus was introduced into Massachusetts, the occurrence of future cases is not a remote possibility. A marked increase in prevalence is, however, extremely unlikely. An awareness of this disease on the part of physicians may disclose additional cases.

Summary

Eight cases of Rocky Mountain spotted fever have been reported from four New England states from 1937 to 1942. Five of these cases had their origin in Massachusetts during the three-year period of 1937 to 1939. The total endemic area in Massachusetts comprises only fifty-nine square miles.

Two cases of Rocky Mountain spotted fever are presented. From one of these the infectious agent was recovered, this being the only case of Massachusetts origin thus far reported from which the virus has been isolated. Neutralizing antibodies were demonstrated in the blood of this patient four and a half years after recovery.

Absence of cases in Massachusetts since 1939 does not necessarily imply a disappearance of the virus, since epidemiologic data acquired in the West demonstrate that the disease may vanish from a localized endemic area for several consecutive years, only to recur.

Although the occurrence of Rocky Mountain spotted fever in Massachusetts may have been the result of an accidental and perhaps transitory introduction of the infectious agent from outside sources, there is a possibility that the virus may have existed here for many years. The relatively few cases suggest that only a small proportion of the ticks on Cape Cod harbor the infectious agent.

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THE ASCORBIC ACID CONTENT OF LATE-WINTER TOMATOES*

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THE tomato is generally considered one of the most important of the protective foods, owing largely to its vitamin content. It is commonly classed as a vitamin C food and is frequently listed as one of the richest natural sources of ascorbic acid (vitamin C). Since it can be raised easily even by amateur gardeners, it is almost universally recommended for the home garden. It is also grown in enormous quantities for commercial canning, and for the manufacture of tomato juice. As a result of this extensive use and great popularity of the tomato, many studies have been made of its ascorbic acid content.

Apparently a number of factors affect the amount of ascorbic acid developed in tomatoes. For instance, Tripp, Satterfield, and Holmes[1] found varietal differences ranging from 14.8 mg. per 100 gm. for John Baer tomatoes to 21.8 mg. for Pritchard, and Maclinn and Fellers[2] report values varying from 9.0 mg. for Pritchard Stokes to 59 mg. for Princess of Wales (Sutton). The reports by Booher, Hartzler and Hewston,[3] Currance,[4] Maclinn, Fellers and Buck,[5] Hamner and Maynard[6] and others who have carefully reviewed the literature indicate that field-grown, fully ripened, vine-matured, summer tomatoes contain about 25 mg. of ascorbic acid per 100 gm. Thus a good-sized tomato of this type could supply nearly half the 75 mg. of ascorbic acid recommended by the Committee on Food and Nutrition of the National Research Council[7] for the daily needs of the human adult.

One frequently finds on the market, however, tomatoes that in neither color, taste nor physical appearance compare with the high quality of the field-grown, vine-matured summer tomatoes. Such tomatoes are commonly found in the stores of the northeastern United States during the late winter and early spring months. Inasmuch as these tomatoes are grown, shipped and sold under conditions quite different from those of the normal, local growing season, it appeared desirable to determine the ascorbic acid content of typical late-winter tomatoes. Such data are of particular interest to the physician, nutritionist and homemaker who wish to ascertain accurately the amount of ascorbic acid supplied by late-winter tomatoes, and the present study was conducted to accumulate these data.

The tomatoes analyzed were obtained from six local stores. Three of these were of the small private or independent type and three were representative of the large chain grocery stores. The tomatoes were purchased in small retail packages or by the pound, just as a homemaker would purchase them for home use.

Samples for analysis were obtained by cutting slices, weighing 10 to 15 gm., through the medial section in the same manner as the tomato is prepared for serving. The assay procedure described by Tripp, Satterfield and Holmes[1] was followed. The skin was quickly removed and the slices immediately submerged in acetic acid and thoroughly macerated by grinding in a mortar with acid-washed sand. Thus, destruction of vitamin C by enzymes was reduced to a minimum. The mix-

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TABLE 1. *The Ascorbic Acid Content of Late-Winter Tomatoes.*

MONTH OF PURCHASE	STORE	WEIGHT PER TOMATO	COST PER POUND	ASCORBIC ACID CONTENT	WEIGHT REQUIRED TO YIELD 75 MG. OF ASCORBIC ACID	COST OF 75 MG. OF ASCORBIC ACID
		gm.	*cents*	*mg./100 gm.*	*gm.*	*cents*
February	Chain A	—	29	8.0	938	60
		93.7	29	4.0	1876	120
	Average	93.7	29	6.0	1407	90
March	Chain A	84.3	29	5.4	1389	89
		92.1	29	7.0	1071	68
		88.1	29	8.0	938	60
	Average	88.2	29	6.8	1133	72
March	Independent A	130.6	36	5.9	1271	101
		92.4	36	7.4	1014	80
		111.0	36	4.4	1705	135
		77.1	36	5.2	1442	114
	Average	102.8	36	5.7	1358	108
April	Independent B	96.0	18	6.7	1119	44
		90.4	18	9.8	765	30
		103.4	18	7.6	987	39
		82.0	18	17.5	429	17
	Average	93.0	18	10.4	825	33
April	Independent C	85.6	33	7.3	1027	75
		93.7	33	9.5	789	57
		101.7	33	8.8	852	62
		65.0	33	8.4	893	65
		102.4	33	12.0	625	45
	Average	89.7	33	9.2	837	61
April	Chain B	74.6	35	10.2	735	57
		75.5	35	12.9	581	45
		113.4	35	4.8	1563	121
		111.0	35	9.4	798	62
	Average	93.6	35	9.3	919	71
April	Chain A	84.4	29	8.1	926	59
		88.3	29	8.0	938	60
		116.7	29	7.3	1027	66
		81.7	29	9.9	759	48
		—	29	7.6	987	63
	Average	92.8	29	8.2	927	59
April	Independent A	102.4	42	16.0	469	44
		48.2	42	10.5	714	66
		93.0	42	13.9	540	50
		59.0	42	12.7	590	55
		71.7	42	14.1	532	49
	Average	74.9	42	13.4	560	53
April	Chain B	75.1	32	8.6	872	61
		86.8	32	13.0	577	41
		93.1	32	10.2	735	52
		84.4	32	11.8	636	45
		75.8	32	10.3	728	51
	Average	83.0	32	10.8	710	50
April	Independent B	77.4	29	6.1	1229	79
		98.7	29	7.1	1056	68
		105.4	29	10.7	701	45
		84.8	29	13.2	568	36
		90.9	29	5.2	1442	92
	Average	91.4	29	8.5	999	64
April	Chain C	71.6	33	6.2	1210	88
		77.5	33	2.5	3000	218
		79.3	33	2.5	3000	218
		100.3	33	3.1	2419	171
		74.7	33	5.8	1293	94
	Average	80.7	33	4.0	2184	158
April	Independent C	105.9	30	9.1	824	54
		93.1	30	9.2	815	54
		95.1	30	4.9	1531	101
		98.3	30	8.3	901	60
		94.2	30	6.0	1250	83
	Average	97.3	30	7.5	1064	70
April	Chain C	98.4	30	5.0	1500	99
		82.6	30	6.9	1087	72
		88.5	30	14.1	532	35
		96.3	30	7.6	987	65
		76.3	30	22.0	341	23
		57.1	30	12.4	605	40
	Average	83.2	30	11.3	842	56
	General averages	88.8	—	8.8	1037	72

ture of finely ground tomato, acetic acid and sand was transferred to a centrifuge tube and spun at 2000 r.p.m. for ten minutes, which produced a clear supernatant liquid. The ascorbic acid content of this liquid was obtained by titration with sodium-2, 6-dichlorophenolindophenol dye to a faint-pink end point.

The results obtained from the assay of 58 tomatoes are reported in Table 1, which also includes data concerning the source, weight and cost, the amount of tomato required to yield 75 mg. of ascorbic acid and the cost of this amount from the tomatoes in question. The average weights of the tomatoes obtained at the thirteen purchases were 93.7, 88.2 and 92.8 gm. for chain store A, 93.6 and 83.0 gm. for chain store B, 80.7 and 83.2 gm. for chain store C, 102.8 and 74.9 gm. for independent store A, 93.0 and 91.4 gm. for independent store B and 89.7 and 97.3 gm. for independent store C. The average weight of all the tomatoes was 88.8 gm. The cost per pound varied from 18 cents for the first purchase from independent store B to 42 cents for the second purchase from independent store A.

The ascorbic acid content of the tomatoes is reported on a 100-gm. basis. It varied widely within each of the thirteen lots as well as between the lots. The average values were 6.0, 6.8 and 8.2 mg. for chain store A, 9.3 and 10.8 mg. for chain store B, 4.0 and 11.3 mg. for chain store C, 5.7 and 13.4 mg. for independent store A, 10.4 and 8.5 mg. for independent store B and 9.2 and 7.5 mg. for independent store C. The average ascorbic acid content of all the tomatoes was 8.8 mg. per 100 gm. The lowest value obtained was 2.5 mg., and the highest was 22.0 mg. for tomatoes purchased from chain store C. This latter value, and a few of those obtained for other tomatoes, are similar to those obtained by a number of investigators for field-grown tomatoes, but the average ascorbic acid content of the late-winter tomatoes, 8.8 mg. per 100 gm., is only about one third that of summer tomatoes. In fact, it is definitely less than the ascorbic acid content of canned tomatoes, which are available at the time late-winter tomatoes are consumed. Daniel and Rutherford[8] found that the ascorbic acid content of tomatoes canned six months previously was 14 mg. for glass containers and 15 mg. for tin containers. Rogers and Mathews[9] compared commercial and home-canned tomatoes and found 13.8 mg. of ascorbic acid for the former and 13.9 mg. for the latter. Hence, it is obvious that whereas the late-winter tomato possesses attractive decorative features for the table, particularly in salad combinations, it does not have the ascorbic acid value of fresh summer tomatoes or of tomatoes canned six months previously.

Obviously, tomatoes cannot be relied on as the sole source of ascorbic acid in the dietary. Nevertheless, for the sake of comparison, an estimation has been made of the amount of these tomatoes that would be required to supply the 75 mg. of ascorbic acid recommended by the Committee on Food and Nutrition of the National Research Council[7] for daily consumption by adult man. The lowest amount of tomato required was 341 gm., or about three quarters of a pound, and the maximum amount required was 3000 gm., or approximately 6½ pounds. It is clear from these values that late-winter tomatoes as ordinarily eaten in the average home can contribute only a small portion of the daily human requirements for ascorbic acid.

The cost of the quantity of tomatoes required to contribute 75 mg. of ascorbic acid to the diet varied from 17 cents for a purchase at independent store B, to $2.18 for tomatoes purchased from chain store C. The average costs for 75 mg. of ascorbic acid in the thirteen purchases of tomatoes were 90, 72 and 59 cents for chain store A, 71 and 50 cents for chain store B, $1.58 and 56 cents for chain store C, $1.08 and 53 cents for independent store A, 33 and 64 cents for independent store B and 61 and 70 cents for independent store C. The average cost of 75 mg. of ascorbic acid from the late-winter tomatoes was 72 cents. It is interesting to compare this cost with 4.8 cents reported by Holmes, Patch and Tripp[10] for 75 mg. of ascorbic acid obtained from oranges available at the same season of the year. Obviously neither the tomatoes nor the oranges would be consumed solely for their ascorbic acid content, but on this basis it is significant that the ascorbic acid content of the late-winter tomatoes cost fifteen times as much as ascorbic acid supplied by oranges purchased at the same season of the year.

Conclusions

It is quite evident from the results of this study that the homemaker, nutritionist and physician must not consider late-winter tomatoes as equivalent to vine-matured, sun-ripened summer tomatoes as a source of ascorbic acid for the human dietary. In computing the vitamin C value of a diet containing late-winter tomatoes, one should not assign to them more than one third the ascorbic acid value ordinarily used for fully ripe, summer tomatoes.

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THE INCIDENCE OF GALLSTONES IN THE HIGHER AGE GROUPS*

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BOSTON

THE post-mortem records of the Long Island Hospital have been examined for the purpose of determining the incidence of gallstones in the higher age groups. The Long Island Hospital is designed for the medical care of the destitute of the City of Boston. The majority of its patients belong to the higher age groups and most of them are of Irish extraction; a minority are of Italian origin and a few are Negroes.

The post-mortem records, 3242 in all, for the years 1900 to 1942, inclusive, were studied with reference to the frequency of gallstones in relation to age, sex and lesions of the gall bladder, and to the question of an increase of cholelithiasis in recent decades.

The results yield only minimum figures because all post-mortem protocols without definite statements regarding the presence of gallstones were listed as negative. Cases of choledocholithiasis were listed as positive because the gall bladder is generally regarded as the sole source of concretions in the extrahepatic bile ducts.

Table 1 shows the incidence of gallstones found in 2791 post-mortem examinations of patients above the age of forty. The incidence increases with age. Below the age of forty, in 451 post-mortem examinations, the incidence was 1.5 per cent. Above the age of eighty, more than a third of the post-mortem examinations revealed gallstones. This steady rise in incidence of gallstones with age (by decades) has been reported by many authors (Crump,[1] Hansen,[2] Hamilton,[3] Gross,[4] Jaffé,[5] Ludlow,[6] Mosher,[7] Naunyn,[8] Ophüls[9] and Scheel[10]) but has been denied by a few (Hesse and Hesse[11] and Ryerson[12]). Belief that cholelithiasis originates at a much earlier period, to become manifest in later life only, finds no support in the Long Island Hospital figures.

TABLE 1. *Incidence of Gallstones, 1900–1942.*

AGE	NUMBER OF CASES			PERCENTAGE WITH GALLSTONES		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
yr.						
41–60	475	340	815	8.4	19.1	12.9
61–80	975	708	1683	16.6	31.2	22.8
81 and over..	154	139	293	26.0	40.3	32.8
Totals ...	1604	1187	2791			20.9
General averages				15.0	28.7	

Table 2 presents figures regarding the association of gallstones and grossly manifest disease of the gall bladder. These are minimum figures because allowance has to be made for the incompleteness of many of the post-mortem protocols and for the varying degree of competency of the persons who made the examinations. Most of the lesions recorded were acute or chronic cholecystitis, fibrosis or hydrops of the gall bladder. There were a few cases of carcinoma (2 in males and 2 in females). Little attention was found to have been paid to cholesterosis of the gall bladder. However, the fact that only 38 per cent of all diseased gallbladders containing calculi showed easily recognizable gross lesions corresponds with other reports — Scheel[10] reporting 33 per cent of gall bladders with lesions and Ophüls[9] (post-mortem material) 38 per cent. These low figures cast some doubt on the surgical dictum that there are no innocent gallstones. Cholecystitis without gallstones was found in about 2.5 per cent of the post-mortem examinations.

TABLE 2. *Incidence of Gall-Bladder Disease in Cases with Gallstones.*

AGE	CASES WITH GALLSTONES			PERCENTAGE WITH GALL-BLADDER DISEASE		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
yr.						
41–60	40	65	105	37.5	26.1	30.4
61–80	162	221	383	45.0	36.2	40.0
81 and over..	40	56	96	37.5	35.7	36.5
Totals	242	342	584			37.5
General averages				42.1	34.2	

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A definite sex difference in the incidence of gallstones, with ratio of almost 2:1 in favor of women, is evident from Table 3. This is lower than the ratios reported by many authors for Europe and the United States: Jaffé[5] gives about 3:1, Mitchell[13] 3.5:1, Courvoisier[14] 3:1, Brockbank[15] above 25:1 and Hurst[16] 5:1. However, Schretzenmayr,[17] of Vienna, Gross,[4] of Leeds, England, and Hamilton,[3] of Adelaide, Australia, give a 2:1 ratio, and Ludlow's[6] Lakeside Hospital (Cleveland) ratio of less than 2:1 corresponds most closely to that reported here. The higher incidence in women has often been attributed to the influence of pregnancy. The marked rise in incidence above the age of fifty (Fig. 1) does not support such a view

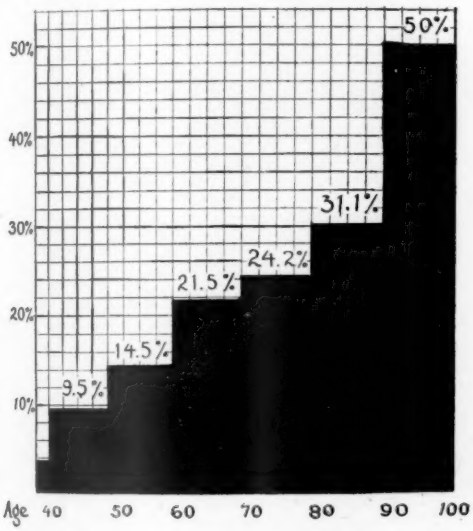

FIGURE 1. *Incidence of Gallstones at Autopsy in Patients over Forty Years of Age.*

and this is also the case with the reports of Scheel,[10] Gross,[4] Hamilton[3] and Lichtwitz.[18]

Comparison of the presence of gallstones in the post-mortem material of the Long Island Hospital from 1900 to 1922 and 1923 to 1942 (Tables 3 and 4) shows a definite increase for the latter period.

TABLE 3. *Incidence of Gallstones, 1900–1922.*

Age	Number of Cases			Percentage with Gallstones		
	Male	Female	Total	Male	Female	Total
yr.						
41–60	204	233	437	4.4	17.6	11.4
61–80	260	355	615	13.0	29.8	22.8
81 and over..	39	61	100	23.0	31.1	28.0
Totals	503	649	1152			18.9
General averages				10.3	24.5	

This increase involved all age groups above forty years and both sexes. The tendency of the sex difference to decrease in recent years is indicated not only by these findings but also by a comparison of the older literature with publications of recent date. Because of the great variation in incidence of cholelithiasis recorded from different countries,

TABLE 4. *Incidence of Gallstones, 1923–1942.*

Age	Number of Cases			Percentage with Gallstones		
	Male	Female	Total	Male	Female	Total
yr.						
41–60	271	107	378	11.4	22.4	14.6
61–80	715	353	1068	17.6	32.5	22.6
81 and over..	115	78	193	27.2	46.8	35.2
Totals	1101	538	1639			22.2
General averages				17.0	32.7	

only figures collected in the same general region are truly comparable. From Chicago, Mitchell[13] in 1918 gave a 3.5:1 ratio, and Jaffé[5] in 1933 a 3:1 ratio. From Cleveland, Ludlow[6] in 1930, gave a ratio of less than 2:1. The reports of Gross[4] and Hurst[16] indicate a similar shift for England.

A high incidence of gallstones is supposed by some authors, including Mosher,[7] to occur in poorly nourished populations. Others, including English,[19] maintain the contrary. The material reported here seems to favor the first view, but from lack of comparable material from higher income groups this question is left undecided.

SUMMARY

The data obtained from post-mortem records at the Long Island Hospital show that the incidence of gallstones increases with age.

Cholecystitis was present in 42 per cent of the males and 34 per cent of the females who had gallstones.

Cholecystitis without gallstones was found in 2.5 per cent of the cases.

A higher incidence of gallstones was found in the 1923–1942 period than in the 1900–1922 period.

The sex difference in incidence of gallstones has decreased in recent years.

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CLINICAL NOTE

KINEPLASTIC AMPUTATION OF THE FOREARM

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KINEPLASTIC amputation for the utilization of muscle power to activate a prosthesis is not a new procedure. Credit for it is due to Kessler,[1] whose work has done much to counteract the indifference and disfavor with which this method was received some thirty years ago. This procedure has a special value at the present time because it may play a leading part in the rehabilitation of those injured in the war.

The purpose of reporting the present case is to emphasize some of the points brought out by Kessler in his various articles. The report also carries a plea to surgeons who do original amputations to bear in mind the possibility that some type of prosthesis will be worn on the stump. In many cases one sees an attempt to save too

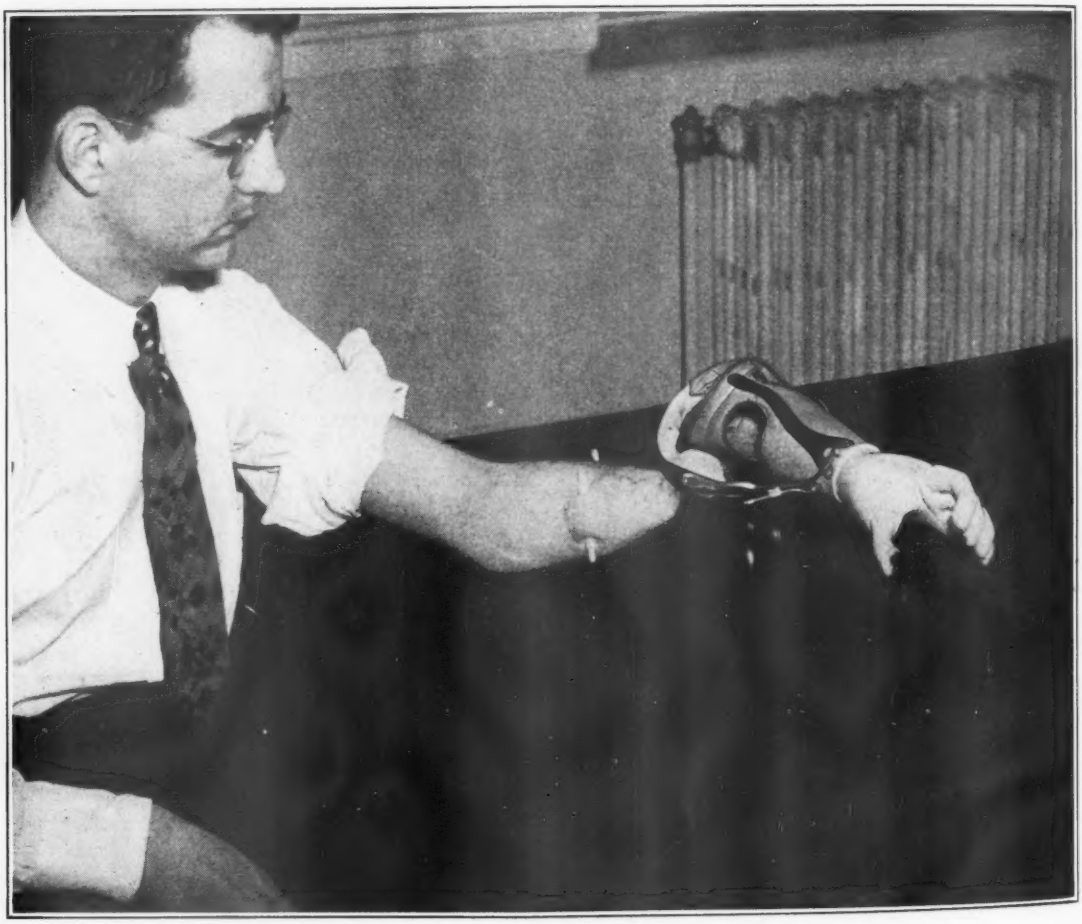

FIGURE 1.
This photograph shows the pins in place, with the prosthesis removed.

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much of the arm, thus leaving a stump that will not adapt itself to any type of prosthesis. As a result, reamputation becomes necessary.

The technic of kineplastic amputation as described by Kessler, although comparatively simple, requires care and precision in several points, as follows:

1. The skin flap should not be over 3.5 cm. square; otherwise there is likely to be some irritation from the pins. Also, one should not pass the skin tube through too much of the muscle belly, and the tendons should of course be avoided.
2. The edges of the skin tube should be carefully closed before it is canalized through the muscle.
3. Excess tension in closing the skin flap should be avoided.
4. The prosthesis should not be applied until all symptoms of discomfort and redness have disappeared from the skin tube.

The only way in which the value of this operation can be shown to a patient is to demonstrate a successful case. The study of photographs and reading matter will not convince him. He must be taught the precise limitation of function that will result from the amputation, and the decision whether it is to be performed should be left to him. The patient must be made to understand that the success of this procedure lies in complete co-operation. To become proficient in adapting oneself to the mechanical principles of a prosthesis takes time and patience. A course of education in the use of the involved muscles should be carried out in the interval between amputation and attachment of the prosthesis.

There are many handicapped people with amputations of the forearm who through years of effort have adapted themselves to devices of every kind, such as hooks and appliances, and who would be unwilling to forsake them for such a procedure as this. Such persons should not be allowed to demonstrate their appliances to the patient until

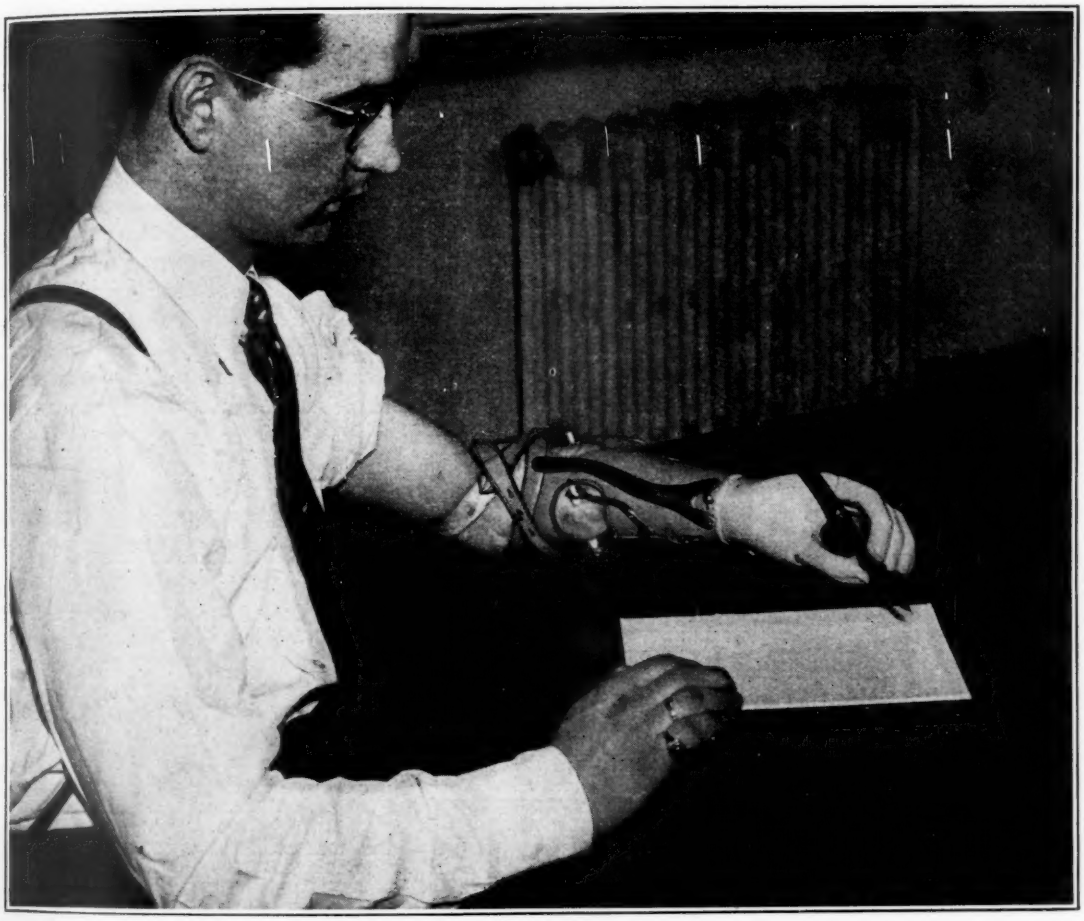

FIGURE 2.

In this photograph the prosthesis has been attached. Note the wishbone and the mechanics of the prosthesis.

he has had an opportunity to see all types of prostheses and devices and to make his own selection among them. Kineplastic amputation has a definite place in such a selection.

Case Report

A. G., a 21-year-old mill hand, was referred by Dr. Harold Kurth, of Lawrence. On October 9, 1941, he caught his left hand in a carding machine. It was practically stripped of soft tissue, and all the bones of the hand sustained multiple comminuted compound fractures. It was impossible to identify the tendons, so that amputation was decided on. This consisted in an ordinary flap amputation, which left a stump measuring 20 cm. from its distal end to the tip of the acromion. The flexor and extensor muscles were fastened to the ends of the amputated radius and ulna and the fascia to give anchorage for flexion and extension. Convalescence was uneventful and the patient returned to work in 3 weeks.

Having heard of Kessler's kineplastic amputation, he asked me to perform one. He was instructed to exercise the stump, going through the motions of closing and opening the fingers so as to develop and train the muscles of the forearm. He was most co-operative and did this religiously.

On March 26, 1942, the kineplastic amputation was done. Two flaps were marked out according to the Kessler technic. The dressing was not changed for 10 days. The skin grafts, which were small, took well. On May 7, measurements were taken and a cast was made, pins having been left in the skin tube for the previous 2 weeks. On July 13, the prosthesis was attached.

At the present time, the patient is working full time. He has become proficient in manipulating his fingers, and is able to pick up his dinner pail, a suitcase, and a cigarette and to hold playing cards in his hand. In other words, following the application of the prosthesis he has learned to activate the artificial fingers with the muscle motors of his forearm as though he had his own fingers. The only complication was a slight irritation of the skin at the edge of the skin tube, which was probably due to the flap's having been made a little too large.

Summary

Kineplastic amputation of the forearm by Kessler's technic is advocated as a valuable and successful procedure.

Complete co-operation of the patient is essential, and there should be preliminary training and exercise of the muscles of the forearm to facilitate function after the attachment of the prosthesis.

A successful case of kineplastic amputation is reported.

43 Bay State Road

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MEDICAL PROGRESS

CANCER: RESULTS OF TREATMENT*

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BOSTON

THERE is still a conviction among the laity and some of the medical profession that cancer cannot be cured or controlled. This pessimism exists in spite of extensive and convincing evidence to the contrary. It is a well-accepted fact that present-day treatment is effective in the early stages of the disease, before it has spread to distant organs or tissues that are essential to life. Moreover, the prognosis is far from hopeless even in more advanced cases. Unfortunately, however, a large proportion of the patients reporting for treatment are still in far-advanced stages. As was stated in a previous report,[1] powerful weapons are available that, if used judiciously and intelligently, will do much to control the disease. Naturally, all look forward to the discovery of an agent that will have a specific action or will enable the body to overwhelm the cancer cell, but even if such an agent is found, it is apparent that it cannot be expected to cure all the cases. In the absence of specific treatment, one should not assume a defeatist attitude regarding present-day therapy, especially since reports in the last several decades reveal an increasing number of cures.

The present report deals with the probability of cure of the commonest forms of neoplastic disease. Although no attempt has been made to review the entire literature of the last ten years, it is hoped that the material cited represents the major contributions. It is a herculean task to evaluate critically each end-result study, but fallacies and discrepancies will be discussed so far as possible. The main purpose is to point out that cancer is a controllable disease; the figures that represent a cross section of the results in the large clinics throughout the world (Table 1) attest to this fact.

Certain fundamental concepts must be defined in order to understand and evaluate the reported statistics. First, what is a cancer cure? It is com-

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monly said that cancer is never completely cured, even though it may remain quiescent. In the case of certain lesions this may be true. However, autopsy findings on patients who die of other diseases and who have no clinical sign of cancer seldom reveal any active disease. Thus, clinical freedom from demonstrable disease must be accepted as the criterion. Perhaps the terms "clinical cure," "free of disease" and "survival without disease" are more applicable. Secondly, what period of time should elapse before one is justified in reporting a clinical cure? Authorities throughout the world have agreed on an arbitrary elapsed time of freedom from disease for five years after the last treatment as a reasonable period to warrant the publication of statements regarding control of the disease. It should be realized that cancer is usually a disease of old age and that a number of patients who remain free of cancer die of intercurrent disease before the prescribed time for reporting the results of treatment. It must be pointed out, also, that in certain cancers a shorter interval is reliable, whereas in others longer periods are necessary. For example, a three-year survival without evidence of cancer is sufficient for lesions involving the oral cavity, since few cases recur after that time and the life expectancy of the patients thereafter is essentially the same as that of the normal population. On the other hand, late recurrences of such lesions as cancer of the breast, ovary and so forth are notorious, thus making a ten-year period more desirable.

In the evaluation of end results many other factors must be considered. Foremost is the natural history of the untreated lesion, for without knowledge of this, the efficacy of treatment cannot be judged.[2–4] The period in which the cases were treated is important, since methods of therapy, especially radiation, have improved markedly in the past twenty years. The stage of disease at the time the patient first comes for treatment alters end results considerably, since some clinics receive a much higher proportion of early cases than do others. Other points of major significance are the histologic criteria of cancer defined by the examining pathologist, the criteria of operability in the various clinics and the judgment and skill of the therapist in choosing and performing the most efficacious form of treatment in the given case. Finally, the method of calculation of end results is probably the greatest single factor in accounting for the differences in the reported figures. Many

TABLE 1. *Reported Five-Year Curability Rates in Common Types of Malignant Neoplasm.*

ORGAN OR TYPE	CURABILITY RATE %	ORGAN OR TYPE	CURABILITY RATE %
Skin	48–68	Gastrointestinal tract:	
Basal cell	38–74	Stomach.	
Epidermoid	39–56	Absolute	5
Breast:		Relative	15–30
Absolute	22–28	Colon:	
Relative	30–51	Absolute	29
Oral cavity:		Relative	38–81
Lip	59–70	Rectum:	
Buccal mucosa	26–31	Absolute	25
Gingivae	27	Relative	38–73
Lower	15–60	Urinary tract:	
Upper	33–74	Bladder	16–55
Palate	23–38	Kidney	19–33
Hard	44*	Male genital tract:	
Soft	20*	Penis	35–40
Tongue	14–37	Testicle	15–53
Floor of mouth	18–32	Prostate:	
Tonsil	15–32	All cases	8
Respiratory tract:		Operable	50–58
Pharynx:		Female genital tract:	
Nasopharynx	18–30	Vulva	26–32
Mesopharynx	15	Vagina	30
Hypopharynx	6–12	Cervix	20–40
Larynx:		Endometrium	35–45
Operable:		Operable (surgery)	48–70
Laryngofissure (early cases)	80	Operable and inoperable (radiation)	35–45
Total laryngectomy	55	Ovary	16–35
Inoperable	27	Sarcomas:	
Thyroid gland:		Malignant melanoma	22–42
Early cases	70	Fibrosarcoma	18
All types	26	Osteogenic sarcoma	19–39

*Three-year rate.

clinics report the absolute cure rate — that is, the percentage of the total number of patients examined who are alive and free from recurrence after a stipulated number of years. All patients who are lost to follow-up examination, whether or not they had disease when last seen, and those who die of intercurrent disease before the specified period are counted as dead of cancer. Untreated and hopelessly advanced cases that receive only palliative therapy are also included in the totals. Since this does not give a true index of the efficacy of treatment, but merely denotes the prognosis for the particular lesion, other methods of reporting have been used. The commonest is the so-called "relative cure" or "determinate cure," but the definition is variable from clinic to clinic. Some clinics include every patient except those who are not treated or who are lost immediately after treatment; others exclude patients in whom no attempt at cure was made, or who were lost to follow-up (even though free of disease), or who died of intercurrent disease. To report that patients were free of disease "from one to ten years" is of little value unless the actual number per year is stated. Even then, recurrence is frequent in the few years after treatment, and inclusion of cases recently treated to increase the number in a reported series is merely confusing. In many instances, a selected group of cases treated by specific methods is published, and this information is of value only in judging the efficacy of such therapy. Thus, it can be seen that reports cannot be directly compared unless the series are of similar composition and the methods of calculation the same. It is obvious that all the above factors must be considered before one can pass final judgment on any single report.

Skin

Cancer of the skin is curable in a high percentage of cases, since the lesions are easily detectable and accessible to therapy by any of the accepted methods. The reports in the literature give credence to this thesis. Magnusson[5] reports three-year cures in 76 per cent of cases of verified skin cancer, as against 75 per cent of those diagnosed clinically. The results in all cases were 75 per cent three-year and 55 per cent five-year survivals without disease. Warren, Simmons and Rea[6] report freedom from disease in clinically diagnosed cancer of the skin without biopsy as 57 per cent for three years and 48 per cent for five years. However, they state that only 16 per cent of the patients were known to be living with cancer or had died from it. Of the remainder, 19 per cent died of intercurrent disease and 16 per cent were lost to follow-up. These are included as failures. As they point out, if the latter two groups, who were free of disease, are included as cured, the survival rate becomes 84 per cent. It is also of interest that in this age group the expected mortality from natural causes is about 25 per cent within the five-year period. Thus, it is impossible to compute the actual curability rate of all patients who enter the clinic.

Histologic Type and Grade of Malignancy

The histologic type and grade of malignancy definitely alter the prognosis of the disease. Basal-cell cancer seldom if ever metastasizes, whereas metastases in epidermoid or squamous-cell cancer are not infrequent. Schuermann[7] reports 74 per cent five-year cures in basal-cell cancers and 45 per cent in epidermoid cancers of the skin. The absolute cure in 401 cases of both types was 68 per cent and the relative cure 85 per cent. Poppe[8] had three-year cures of 73 per cent and 55 per cent in basal-cell and epidermoid cancer, respectively, and 87 per cent in mixed types. McDowall[9] states that in his series 234 (60 per cent) of 390 cases of epidermoid cancer and 310 (70 per cent) of 440 cases of basal-cell cancer were free of disease, but this refers only to primary healing and does not give the true end results. Warren and Hoerr[10] reported 39 per cent five-year cures for epidermoid cancer, of which 44 per cent were in low-grade and 24 per cent in high-grade lesions. The mortality rate from cancer only was 27 per cent in low-grade and 51 per cent in high-grade lesions. The combined mortality rate from cancer only was 32 per cent, whereas the remainder, who were not included as cured, either died of intercurrent disease, were observed for less than five years or were lost before the specified period. Warren, Gates and Butterfield[11] studied the various types of basal-cell cancers and found 38 per cent five-year cures. The method of reporting was similar to that used in a previous study.[6]

Clinical Type and Site of Cancer

Halberstaedter and Simons[12] pointed out that if the lesion was superficial the curability was 83 per cent, but if it was infiltrating the rate dropped to 37 per cent. The survival rate in lesions of the exposed portions of the skin, such as the face and hands, is generally higher than in those elsewhere.[10, 13]

Breast

Most end-result studies deal only with operable lesions, so that the actual prognosis for all cases is considerably lower than that usually reported. The criteria of operability as well as the methods of therapy vary in the different clinics. Other factors are important, such as the stage and histologic type of the disease and the tendency for the lesion not only to invade the lymph nodes but to metastasize to distant organs. However, the re-

sults in any operable series are sufficiently good to warrant optimism regarding the treatment. In treatment, some clinics use surgery or radiation alone, whereas others combine the methods in various ways. The value of supplemental radiation is still debatable, but there should be no question concerning the type of surgical procedure to be performed. Some writers[14, 15] have suggested that simple mastectomy alone or perhaps combined with radiation gives results comparable to those in lesions treated by more radical operations. The reasoning is based on observations of a highly selective group of patients, poor follow-up studies and fallacious suppositions. These writers maintain that the prognosis is so poor in the presence of lymph-node metastases that there is little to be gained by rigorous therapy. The results of therapy in the leading clinics completely refute these arguments. In the first place, the operative mortality of radical mastectomy is seldom more than 2 to 3 per cent, so that on this score alone one cannot justifiably withhold the radical operation. Secondly, the curability rate by radical surgery in cases with axillary metastases is sufficiently high to prove conclusively that it will save many lives. Thirdly, the clinical appraisal of axillary metastases is notoriously fallible and the curability by any method of radiation is exceedingly low. Consequently, one cannot be sure that simple mastectomy will completely eradicate the disease even in the absence of clinically demonstrable metastases. Fourthly, it is essential to remove the pectoral muscles even in the absence of axillary disease, since they are sometimes invaded by the tumor. Fifthly, the proportion of patients entering any clinic with axillary metastases and even more advanced disease is much higher than that of patients in whom the lesion is confined to the breast alone.

It has been found that in untreated cases approximately 15 per cent of the patients were still living six years after the discovery of the disease.[2, 4] The delay in therapy in a study of cases treated before the last decade averaged about a year; it is less at the present time. The life expectancy from onset of over 1500 cases in all stages and treated from either a curative or a palliative standpoint reveals that 28 per cent were still alive six years after onset.[4] Hence, taking all cases into consideration, therapy of any kind seems to improve the prognosis. However, the figures improve still more when only the operable lesions, treated by appropriate radical measures, are considered. In contrast to many types of cancer, those of the breast have a tendency to produce late metastases. Consequently, for ideal end-result studies at least a ten-year period should elapse after treatment. The five-year figures, however, give an accurate index of the prognosis of the treated lesion.

Five-year end results for operated cases range from 30 to 51 per cent[16–32]; the absolute curability for all patients who have treatment of any kind (palliative or curative) is 22 to 28 per cent.[4, 21] When the disease is confined to the breast, the five-year survivals range from 55 to 80 per cent and the ten-year survivals from 36 to 70 per cent. Involvement of the axillary nodes lowers the curability, but the rate is still far from poor. Representative results range from 18 to 45 per cent for five years and from 9 to 18 per cent for ten years. The extreme rates are unusual, for in most cases the results are about midway between them. The radical operation is fairly well standardized, so that except in those clinics where less radical procedures are carried out, the differences in results are due in large part to the criteria of operability. Thus, it can be easily seen that the radical operation is to be preferred and that it should be carried out whenever possible in spite of the fact that a few highly selected cases do almost as well by less radical measures. The merits of radiation alone or in combination with surgery have been reviewed by Brunschwig.[33] He concluded that the possible beneficial effects of preoperative radiation are vitiated by the morbidity resulting from the subsequent operation in a field so irradiated. He further stated that there was no evidence that postoperative radiation increases the survival rate if the disease is confined to the breast, but that it may possibly increase the rate in cases with axillary lymph-node involvement.

Oral Cavity and Respiratory Tract

The degree of curability in cancers of the oral cavity and respiratory tract varies considerably with the site of origin of the primary lesion. In general, those lesions that arise in the anterior portion have a much higher rate of cure than those situated more posteriorly. Many factors account for these differences, most important of which are the histologic grade of malignancy, — the more anterior lesions are usually of lower grade, — the size of the lesion, the mobility of the part, accessibility for treatment and the extent of lymphatic drainage. Recurrence of the primary lesion or the appearance of metastases is rare after three years of freedom from disease,[4] although the tendency to the formation of multiple new cancers is relatively high.[34] Much of the advance in the therapy of lesions of the oral cavity and respiratory tract is due to the splendid work of Coutard,[35] who advocated the protracted type of radiation. This principle used elsewhere in the body has also resulted in the eradication of cancers that would

otherwise have been considered hopeless. It has its greatest value in the treatment of inoperable disease, particularly that involving the tonsils, pharynx and larynx.

Lip

The end results in cancer of the lip include only those lesions that arise on the mucous membrane. Those that appear first on the skin of the lips and invade the mucous membrane secondarily may behave like true lip cancers, but in actuality are skin cancers. Reports of five-year cures range from 59 to 70 per cent, but include both absolute and relative figures.[36–45] Subdivision of results into cases with and without lymph-node metastases gives a better idea of the prognosis in the single case. If the nodes are not involved the curability rate is approximately 85 per cent, whereas with nodal metastases it declines to between 30 and 40 per cent. The uniformity of excellent results from the different clinics is striking and encouraging, in spite of the fact that variations exist in the methods of calculation and therapy. In each instance the series is large, so that the type of case coming to the clinic is not of prime importance. It can likewise be pointed out that most cancers of the lip are of a low grade of malignancy and of relatively small size and that metastases occur in from only 15 to 25 per cent of cases[45] so that most lesions are favorable for cure.

Buccal Mucosa

The lesions of the buccal mucosa comprise those in which the primary site of origin is the inside of the cheek. Extension of disease to adjacent structures greatly influences the prognosis. Lesions that arise in the anterior portion are most favorable for cure. There are relatively few papers on this subject alone, but taken together they represent a sufficient number of cases to be significant. The five-year curability rate ranges from 26 to 31 per cent, and again the uniformity of results is striking.[45–48] The curability rates in cases without metastases approaches 50 per cent, whereas in those with nodal involvement it is approximately 25 per cent, provided cure of the primary lesion is accomplished.[45]

Gingivae

Reports on cancers of the gums should include only those lesions that arise from the mucous membrane overlying the upper and lower alveoli. There is relatively early invasion of the adjacent structures, since the ridges are narrow. This characteristic in itself markedly alters the prognosis. In contrast to lesions of the lip and buccal mucosa, there is a considerable disparity in the end results. Much of this is probably due to the definition of the actual site of origin. In some series only those lesions that are entirely confined to the gingivae are included, whereas in others, regardless of the extent of disease or the site of origin, all lesions involving the gingivae are taken into consideration. When the disease has extended beyond the gums, the site of origin is sometimes difficult to determine.

Curability rates for lesions of the lower gingiva vary from 15 to as high as 60 per cent,[45,47–52] and for the upper gingiva they range from 33 to 74 per cent.[45, 51–54] The figures at the lower extreme usually represent absolute cures, whereas the others are relative rates. This does not entirely explain the discrepancies, and it is not likely that the great differences are due to variations in the technic of therapy alone. The discrepancies would be partially rectified by a definitive method of reporting the actual extent and type of disease.

Palate

In the evaluation of results in this type of cancer, lesions of the hard palate should be separated from those of the soft palate. Lesions of the former are usually less malignant and arise in an immobile part where there is a sparsity of lymphatic drainage. As elsewhere, invasion of adjacent structures alters the outlook. In many cases it is difficult to determine the site of origin, but this is of no practical significance, for if the soft palate is invaded, the lesion behaves as though it had arisen there. Few reports concerning the curability of the lesions are available. In studies restricted to epidermoid carcinoma, three-year cures for lesions of the hard palate were 45 per cent and for those of the soft palate were 20 per cent.[45] The combined figures for epidermoid cancer of the hard and soft palates range from 30 to 38 per cent.[45, 55] When considered from the standpoint of histologic type, the five-year rate has been reported as 88 per cent for adenocarcinoma and 38 per cent for epidermoid carcinoma by one group,[55] and 23 per cent for all types of malignancy by another.[56]

Tongue

Only those cancers that are confined to or arise primarily in the tongue are included. Some authors do not distinguish lesions of the tongue and floor of the mouth, but this is usually satisfactory since there is little difference in their behavior. The position of the primary lesion is important, since lesions of the anterior portions are usually less malignant. The lesions metastasize early, owing in large measure to the relatively high grade of malignancy, the muscular action of the tongue and the abundance of lymphatics. End-result studies from a large number of clinics reveal variations in five-

year cures from 14 to 37 per cent.[45, 48, 50, 52, 57–66] Most figures, however, are approximately midway between the extremes — that is, 25 per cent. Cures as high as 50 per cent have been obtained for cancers of the anterior third of the tongue, whereas those for the base are as low as 5 per cent.

Floor of Mouth

There are few studies restricted to lesions arising solely in the floor of the mouth. In this group, five-year cures from 18 to 32 per cent have been published,[45, 48, 50, 67, 68] but as in cancer of the tongue, most figures are an average of the extremes (25 per cent). The same factors that operate in the prognosis of cancer of the tongue should be considered in lesions involving the floor of the mouth.

Tonsils

Lesions of the tonsils are highly malignant and, as is to be expected, the curability rate is low. Frequently the first sign noted by the patient is a swelling in the neck caused by lymph-node involvement. Most observers[35, 48, 69–72] report the five-year rate to be about 18 per cent, although two clinics[48, 69] had rates as high as 30 and 32 per cent. The latter figures are well substantiated, and in this instance it is likely that the methods used represent a definite advance in therapy.

Pharynx

The pharynx is anatomically divided into the nasopharynx, the mesopharynx (the oropharynx, which in reality includes the soft palate and the fauces) and the hypopharynx. As in the case of the tonsils, the first sign may be a swelling in the neck.

The curability rates of cancer of the nasopharynx for five years of 30, 25 and 18 per cent have been recorded.[35, 73, 74] The average five-year survival rate of lesions of the mesopharynx has been reported as 15 per cent.[75] The results of treatment in cancer of the hypopharynx are extremely poor and range from 6 to 12 per cent[35, 48, 76, 77]; these figures were confined to lesions that arose primarily in the hypopharynx.

Larynx

Confusion in the evaluation of end results in cancer of the larynx exists because of differences in the definition of the terms "intrinsic" and "extrinsic." True laryngeal lesions are those that arise in the cavity itself and are intrinsic. Subsequent extension to include the aryepiglottic fold, the pyriform fossa or the postcricoid region — which are in reality parts of the hypopharynx — makes it difficult in many cases to determine the primary site of origin. When tumors arise outside of the cavity but in juxtaposition, they are really hypopharyngeal cancers, but have been called extrinsic lesions of the larynx by many observers. Once the lesion extends beyond the laryngeal cavity, it behaves like lesions that arise in the hypopharynx, so that this differentiation is not significant. Intrinsic lesions, which arise in and remain confined to the larynx, are usually operable, whereas those that extend beyond or arise in the hypopharynx are seldom amenable to surgical removal.

In the previous section, cancers arising in the hypopharynx were considered, but the figures presented below refer not only to those lesions that are truly laryngeal but to those that extend outward to involve adjacent structures as well. The curability rate of intrinsic cancer of the larynx is relatively high. In the operable group treated by laryngofissure — obviously very early lesions — the five-year rate averages about 80 per cent.[52, 78, 79] One group[80] reports 96 per cent survivals without disease from two to thirteen years. The results of total laryngectomy average about 55 per cent. The results of therapy in the inoperable group are much lower, but considering the extent of disease in many cases the results are encouraging. For example, Coutard[81] reports 27 per cent five-year cures. It must be remembered that the lymphatic drainage of the true larynx is relatively sparse, whereas that of adjacent structures, including the hypopharynx, is exceedingly rich. Thus, regional lymph-node metastases are much less frequent in the former (18 to 35 per cent) than in the latter (56 to 74 per cent).[45] It is not surprising that differences in prognosis have been observed between intrinsic and extrinsic lesions of the larynx. The smaller size of the former, the barrier exerted by the laryngeal cage to extension of disease and the lower incidence of lymph-node metastasis are the main factors accounting for this.

Thyroid Gland

Cancer of the thyroid gland is frequently discovered after routine thyroidectomy for other reasons. The prognosis in the cases without clinically demonstrable cancer is excellent, whereas those lesions that are suspected or are detected before operation have a much lower curability. The prognosis is also altered by the frequency of blood-vessel invasion, nodal metastases and dispersion to distant organs. As in the case of cancer of the breast, end results for periods longer than five years are desirable. Portmann[82] reports 27 per cent five-year survivals in 200 consecutive cases, whereas DeQuervain[83] found 31 per cent in a group of lesions diagnosed clinically and subjected to radical operation. Pemberton[84] had 70 per cent five-year cures in a series of cases in which the lesion was found incidentally or was suspected at operation. As emphasized by Lahey et al.[85] and by Pemberton,[84] the prognosis also varies considerably with the histologic type and mode of spread.

The curability is most favorable in papillary adenocarcinoma, in which the rate is as high as 80 per cent, as contrasted with diffuse carcinoma, small-cell or giant-cell carcinoma or sarcoma, where the rate is 20 per cent or less. Fortunately, many of the cases belong to the more favorable group, so that the general prognosis is good.

Gastrointestinal Tract

It is the opinion of most people that cancer of the gastrointestinal tract is a hopeless disease. Early diagnosis is sometimes difficult and seldom made, especially since patients minimize their symptoms and usually do not report for examination until the disease is relatively advanced. This is truer for cancer of the stomach than for lesions of the colon and rectum. In spite of these shortcomings and considering the magnitude of the procedures in operable cases, the end results are excellent. In recent years, the operability rates for all lesions have risen, which augurs well for the future. At the same time, the mortality rate for radical procedures is declining, because of a better acquaintance with technics and preoperative and postoperative management. Variations in the reported results depend to a large extent on the criteria of operability of the various clinics, the operative mortality and the stages of disease comprising the series reported. Some clinics attack only relatively early lesions, whereas others attempt heroic procedures in an effort to cure the disease. At any rate, it is clear that cancer of the gastrointestinal tract in the operable stage is a curable disease.

Stomach

Approximately 50 per cent of all patients with cancer of the stomach are operable, but actually only about a half of these are suitable for radical curative procedures.[86-90] In reality many of these are borderline lesions. The five-year curability rate of all cases that enter the hospital is about 5 per cent.[87, 88] However, the prognosis in resectable lesions is much brighter in spite of operative mortalities ranging from about 15 to 30 per cent.[86-91] The rates of survival in this group as reported in large series vary from 15 to 30 per cent, although most of the results are between 20 and 25 per cent.[86-98] Some of the figures include operative mortality, whereas others pertain only to those patients who survive the operation. If the lymph nodes are not involved, five-year survival rates range from 45 to 62 per cent, but decline to 18 per cent when the nodes are involved and to about 10 per cent when the neighboring organs are invaded.[86-89]

Colon

The operability rates in cancer of the colon are fairly high, but the criteria vary in the different clinics. In recent years, it has been reported as being from 55 to 85 per cent, although the higher figures in this range are unusual.[99-105] The operative mortality ranges from about 12 to slightly over 20 per cent.[99-105] The higher rates may have been partially due to attempts to cure patients who were not in the best of physical condition or in whom the disease was fairly extensive. Staging of the operation also alters the mortality rate.[99-101] In general the two-stage procedures have a lower mortality. Ochsner and DeBakey[105] collected the statistics from the literature and found that the operability in different clinics varied from 38 to 81 per cent but averaged 59 per cent. In 2991 collected cases the operative mortality was 22 per cent and the curability rate in nearly four thousand reported resections ranged from 41 to 53 per cent. An absolute cure of 29 per cent has been reported by Cattell and Sugarbaker.[104] There is a definite uniformity of five-year survivals in patients whose lesions were subjected to resection. In clinics caring for large numbers of cases, most figures range from 47 to 56 per cent.[99-109] The site of the lesion is important. Five-year survivals for cancers of the right colon range from 51 to 71 per cent,[99, 102, 107, 110] for the transverse colon average about 40 per cent,[99] and for the left colon average about 38 per cent.[99, 102, 107] The degree of mural penetration and the grade of the tumor must be considered, especially in relation to lymph-node metastases.[111] In the absence of positive nodes, the five-year rate for all cases is as high as 63 per cent and only declines to approximately 45 per cent when the nodes are involved. Lesions of low-grade malignancy have the highest curability. For example, it has been reported that Grade I lesions without metastases are curable in 69 per cent of operated cases, as contrasted with 37 per cent in Grade IV lesions. If the lymph nodes were invaded, the survival rates were 55 and 15 per cent, respectively.[103]

Rectum

The operability rate of cancer of the rectum has increased and the operative mortality has declined because of the great advance made in operative treatment, largely through the efforts of Miles, Jones, Lahey and others. The operability rate in cancer of the rectum at the present time ranges from 50 to 75 per cent[100, 101, 104, 112] and the operative mortality varies from 7 to 13 per cent (average 10 per cent).[100, 101, 104, 112-115] Cattell and Sugarbaker[104] report an absolute curability of 25 per cent, but the five-year rates on resectable cases range from 38 to as high as 73 per cent.[100-104, 108, 112-117] The latter figure is unique and is based on a selected group of patients. Most figures approximate 45 per cent.

Urinary Tract

The two commonest sites of cancer in the urinary tract are the bladder and the kidney. Lesions of the urethra and ureter are relatively rare. Therefore, only the former lesions will be considered.

Bladder

There are a variety of forms of cancer of the bladder, and although many are slowly growing, in general the disease is very lethal. Here as elsewhere, the curability depends on the type and extent of the disease, the grade of malignancy and the degree of radiosensitivity and operability. The method of therapy varies from electrocoagulation or radium implantation for the smaller lesions to partial or complete cystectomy for operable cancer, and to x-ray therapy only for the more advanced cases. The American Urological Association has established a registry for bladder cancer as an aid to better diagnosis and treatment. Ferguson et al.[118] analyzed the reports on 658 cases sent into the registry and found that five years following operation 23 per cent were living, but that only 16 per cent were free of disease. Since these were operable lesions, the group must be considered as those favorable for cure. Reports from single clinics usually deal with the results of treatment by different methods or according to the type of lesion. Obviously this represents selection of cases, so that it is difficult to evaluate the actual prognosis of bladder cancer as a whole.

In lesions amenable to local radium implantation, the recent five-year cure rates vary from 38 to 44 per cent.[119–121] Only 10 per cent of the more advanced cases, treated by x-ray alone, survive without disease five years after treatment.[122] Five-year cures of infiltrating cancers of the bladder are as high as 55 per cent if treated by total cystectomy, but are only 18 per cent when partial cystectomy is done.[123] Barringer,[124] in a comprehensive study of 257 patients undergoing all types of therapy, found a 40 per cent five-year relative rate (based on 211 cases) and an absolute rate of 33 per cent. If the lesion was of papillary character, the relative cure was 56 and the absolute cure 45 per cent; if infiltrating, it was 29 and 25 per cent, respectively.

Kidney

There are few recent reports on cancer of the kidney, and these have to do with favorable lesions. Smith[125] combined various reports and quotes a five-year survival rate of 19 per cent. The figures of Hyman[126] and of Beer[127] are almost identical. They found an operative mortality of about 10 per cent and a curability rate of 33 per cent of the survivors. Priestley[128] reported that 38 per cent of patients with hypernephroma, 35 per cent of those with epidermoid cancer of the renal pelvis and 20 per cent of those with Wilm's tumor (adenofibrosarcoma) survived for five years following operation.

Male Genital Tract

Cancers of the male genital tract, except those involving the penis, have a low curability rate, especially since few patients present themselves for treatment in the early stages. Furthermore, cancers of the testicle and scrotum are usually highly malignant, whereas cancer of the prostate, although usually quite slowly growing, seldom causes symptoms until the disease is fairly well advanced. Since cancer of the scrotum is fairly rare, it will not be discussed.

Penis

Cancer of the penis behaves like that of the lip regarding its mode of growth, grade of malignancy and propensity to metastasize. Many patients, however, report for treatment when the disease is advanced, so that the chances for cure are less favorable. The usual five-year curability rates range between 33 and 50 per cent[45, 129–132]; in highly selected and favorable cases they are as high as 75 per cent.[133] The rate is about 60 per cent in the cases without lymph-node involvement and declines to 25 per cent when lymph nodes are invaded. If cure of the local lesion is obtained in the latter group, the curability rises to 42 per cent.[45]

Testicle

Cancers of the testicle except for the teratomas are usually highly malignant and metastasize early to the regional, periaortic and thoracic nodes as well as to distant organs. Chorioepitheliomas are the most malignant, and cures are seldom recorded. Dean[134] found 29 per cent of five-year cures in 170 cases of all types of testicular tumor. In 23 without demonstrable metastases, however, the rate was 79 per cent. Smith et al.[135] reported 15 per cent of their patients as alive and well two years or more after treatment. Higgins and Buchert[136] state that five years is not a long enough follow-up period to establish the final result and report 14 per cent ten-year cures. Leddy and Desjardins[137] report 53 per cent five-year survivals in obviously selected cases, and state that in cases without metastases at the time of treatment there is a 60 per cent chance of surviving five years or longer, whereas other cases have a 30 per cent probability. Payne[138] found 40 per cent of 38 cases free of disease for five years.

Prostate

Until the advent of castration and the use of estrogenic hormones in the treatment of cancer of the prostate, the curability rate was exceedingly

low.[139] A considerable time must elapse to evaluate the efficacy of this new treatment, but there is no question that as a palliative, even if not a curative, measure it greatly increases the life expectancy of men suffering from this disease. It is unusual to detect the lesion in its early stages, and many are found only after prostatectomy for clinically benign hypertrophy. Barringer's[140] figures from an unselected group of cases demonstrate strikingly the stage of disease when his patients were first seen. Less than 5 per cent of the tumors were small, 7 per cent were medium, and 88 per cent were classed as large. The series included 351 patients, of whom only 8 per cent of 322 followed were living and well for three to seventeen years. Smith[141] reported 28 per cent living from one to five years or more in early and moderately advanced cases treated by total perineal prostatectomy. In early cases selected and treated by the same operation, the following percentages of five-year cures have been recorded: Belt,[142] 58 per cent; Young,[143] 53 per cent; and Colston,[144] 50 per cent.

Female Genital Tract

Comprehensive reports of the results of many clinics in cancer of the female genital tract have been published by Meigs[145] and by Morton.[146] Consequently, the reader is referred to these publications for details. The lesions differ considerably in histologic type, in radiosensitivity and in accessibility for treatment by radiation or surgery. Hence, treatment for each lesion is governed by these considerations. Only the commoner lesions are discussed below.

Vulva

Cancer of the vulva usually occurs in the older age groups and is usually of squamous-cell origin. These lesions as a rule do badly with radiation, so that they are essentially a surgical problem. The lesions frequently grow rapidly, metastasize freely and early to the regional lymph nodes, and have a great tendency to develop local recurrence. The development of new primary cancers in the same region after previous vulvectomy is not unusual. Representative five-year cure rates vary from 26 to 32 per cent.[147–150] All authors agree that the early lesions yield a high percentage of cures, but there is a considerable decline when the nodes are involved.

Vagina

Reports on the cure of cancer of the vagina are scarce. In general the curability rate is quoted as 30 per cent.[151]

Cervix

Cancer of the cervix is the commonest form of cancer of the female genital tract and is usually of squamous-cell origin. It spreads early to adjacent structures, such as the vagina, broad ligaments and uterine cavity; in addition, it metastasizes freely to the regional lymph nodes. A number of classifications have been proposed to facilitate evaluation of the end results. This is essential because of the marked differences in the stage of the disease when the patient is first seen. Except for minor variations all are in essential agreement. The stages are roughly classified as:

Stage I. Confinement of disease to the cervix.

Stage II. Involvement of the vagina or extension into the uterine cavity.

Stage III. Extension to one or both broad ligaments.

Stage IV. Fixation of the uterus, or wide extension into both broad ligaments or into the bladder or rectum, or distant metastases.

The literature on cancer of the cervix is voluminous. Since the lesions are usually radiosensitive, there are a large number of papers dealing with the relative merits of operative versus radiation procedures in the treatment of the more favorable cases (Stages I and II). The reports from most clinics, however, reveal that the greatest number of cases are first seen in the more advanced stages. The majority of reports of five-year end results for all stages combined vary from 20 to 40 per cent.[152–175] These differences are partially accounted for by the method of reporting and by the percentage of each stage in any one clinic. The average report reveals figures midway between the extremes. Five-year cures by stages are as follows, the lowest figures usually representing absolute cures: Stage I, 40 to 80 per cent; Stage II, 34 to 65 per cent; Stage III, 13 to 35 per cent; and Stage IV, 0 to 8 per cent.

Although radiation is used almost entirely in some clinics, there are many advocates of radical hysterectomy (Wertheim, abdominal route, or Schauta, vaginal route) for the earlier cases. One of the major indications is the removal of lymph-node metastases, which ordinarily are not only resistant but also inaccessible for adequate irradiation. So far as the local lesion is concerned, either radiation or surgery is an efficient method of therapy. Occasionally an early lesion is radioresistant, and in these cases surgical removal can usually be done subsequently. Bonney,[154] who advocates Wertheim hysterectomy, found an operability rate of 63 per cent and reports five-year cures of 40 per cent; in cases without nodal involvement the curability rate was 53 per cent, and in those with nodal metastases, 22 per cent. This is to be compared with the results of radiation, especially since the mortality is higher from operation (average 15 per cent) than from radiation (usually less than 3 per cent), even in the most skilled hands. There-

fore, this must be balanced in judging the efficacy of any therapy. Nevertheless, it is apparent that no one form of therapy suffices for all cases, and as in cancer elsewhere, the decision concerning the merit of any treatment should be made in the given case.

Fundus of Uterus

Cancers of the endometrium are usually adenocarcinoma and differ considerably in their radiosensitivity. The lesions may remain confined to the uterine cavity for a long period of time before they penetrate the myometrium or spread to the cervix. Metastases to lymph nodes occur relatively late in the disease. The usual treatment of the operable lesions at the present time is total hysterectomy. The inaccessibility of the lesion for local radiation therapy, the difficulty in determining the exact site of origin and the frequent radioresistance of the lesions favor the employment of surgical procedures wherever possible. However, cures in operable cases may be obtained by judicious radiation therapy. Many clinics now combine the methods by inserting radium into the uterine cavity and subsequently performing a hysterectomy.

The curability for operable cancer of the endometrium treated by hysterectomy alone or combined with radiation is high; that of the inoperable group is quite low. Statistics do not as yet prove the value of complementary radiation in surgically treated cases. Five-year survival rates, including therapy of all types in all cases, average about 40 per cent (range 35 to 45 per cent).[157, 161, 167, 176–185] Hysterectomy alone or in combination with radiation yields cures of 48 to 70 per cent in the operable group, whereas radiation alone — including both operable and inoperable cases — produces relative cures of 35 to 45 per cent. The published figures comparing the relative merit of surgery and radiation in operable cases favor the former, but this is to be expected, since the operative mortality is low (2 to 4 per cent) and eradication of the disease is more certain. Nevertheless, in poor-risk patients and in the inoperable group, radiation can be expected to give good results.

Ovary

There are a number of histologic types of cancer of the ovary. Difficulties in the classification of these tumors exist because of variations among the forms. The rate and mode of growth are of particular importance in the curability of the lesions. Encapsulated tumors offer the greatest chance for cure. When the cancer has spread beyond the ovary and cure cannot be attained, the survival rate with disease present may still be considerable, since many of the lesions are slowly growing. Furthermore, some of the tumors are radiosensitive, so that the life expectancy without cure may be further increased by radiation. Unfortunately, the tumors seldom produce symptoms until the process is fairly well advanced, so that the over-all curability rate is not so high as one would hope.

Meigs[186] reports a 16 per cent 5-year survival rate. This figure is absolute regarding the prognosis of all types of ovarian cancer after treatment. Early cases have a higher curability rate. Lynch[187] points out that because of the individual characteristics of growth, the five-year period is inadequate for evaluation of cure. Recurrence of slowly growing tumors may not be detected before this interval, thus making estimation of clinical cure difficult. His figures reveal a 35 per cent five-year survival rate following treatment. Walter et al.[188] discuss the merits of radiation in conjunction with surgery. Their five-year results for treatment with surgery alone were 6 per cent, with surgery and inadequate radiation 10 per cent, and with adequate radiation 29 per cent. These figures are difficult to assess, since the terms "inadequate" and "adequate" are matters of definition.

Sarcomas

In general, the curability of sarcomas is low, except when the disease is treated in the early stages. Even then control of these lesions is difficult because of the great tendency to metastasize through the blood stream.

Malignant Melanoma

Malignant melanoma metastasizes freely by way of either the lymphatics or the blood stream. It is radiosensitive in about 10 per cent of cases. The criteria of malignancy used by the pathologist are of major importance in the end-result reports. Five-year curability rates vary from 22 to 42 per cent.[45, 189–192] As in other reported series, most of the figures are midway between these extremes.

Fibrosarcoma

Fibrosarcoma rarely metastasizes through the lymphatics, but it is difficult to eradicate locally and spreads freely through the blood stream. Three-year cures average about 21 per cent, whereas the five-year rate is approximately 18 per cent.[193–196]

Osteogenic Sarcoma

The American College of Surgeons has established a registry for bone tumors for the purpose of verifying the diagnosis, for evaluating the various forms of treatment, and for a better understanding of the course of the disease. There is a wide variation in the histologic type and in the site of origin. The accessibility for treatment and the frequent blood-stream metastases influence the

prognosis. Reports reveal five-year survival rates in favorable cases of 19 to 39 per cent (average 30 per cent).[197–202] The higher results refer to those most suitable for operative treatment. The results in all cases are obviously lower, but the figures are of importance as indicating that treatment of the disease is not hopeless.

Malignant Lymphoma and Hodgkin's Disease

The lesions of malignant lymphoma and Hodgkin's disease are usually highly malignant and very radiosensitive. As a result, even though the eventual curability rate is exceedingly low, the prolongation of life by radiation is considerable. Variability in histologic type and the mode of spread of the individual forms frequently alter the prognosis.[203, 204] Several reports reveal that in certain types of the diseases a number of patients survive for five years and that in some cases the disease has been completely controlled.[203–206]

Other Organs

It is too early to appraise the results of the newer concepts of treatment of such cancers as those of the esophagus, lungs, duodenum, bile ducts and pancreas. Formerly these lesions were considered as hopeless, but as previously pointed out,[1] the recent rapid strides in surgical treatment offer hope of a cure of a reasonable number of patients.

* * *

The present-day treatment of cancer is effective in controlling the disease in its various manifestations. In several forms the rate of cure is even higher than that of some other diseases. It cannot be emphasized too strongly, nor be repeated too often, that the prevention, early diagnosis and treatment of cancer are the means to a better curability rate. Palliative therapy for the more advanced lesions is of great value in the prolongation of life and in the alleviation of suffering in the final stages of the disease.

Variations in the methods of reporting end results make it difficult to gauge accurately the curability rates in the different types of cancer. Nevertheless, even at present, it is clear from a careful analysis of the statistics of clinics throughout the world that there is a fairly good agreement in the survival rates. It is hoped that more uniform and complete methods of reporting results will be adopted, so that series of cases from each clinic can be compared directly, which may lead to more efficient therapy.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29371

PRESENTATION OF CASE

A thirty-two-year-old housewife was admitted to the hospital because of stupor and convulsions of eighteen hours' duration.

For the past ten years the patient had had bronchial asthma, for which she had been repeatedly admitted to this hospital. No definite causative agent could be identified, but she was known to be sensitive to morphine, codein, aspirin and barbiturates, and she had been taught to give herself adrenalin subcutaneously and aminophyllin intravenously. During her fifth admission, five and a half years prior to the present one, she had had an attack of violent abdominal pain associated with diarrhea. At that time the spleen was found to be "easily palpable." The abdominal pain cleared up without residual, and during the next eight months, when she had been examined repeatedly in the Out Patient Department, the spleen had not been felt. The sixth hospital admission had been occasioned by a miscarriage at three months, from which she recovered uneventfully. The seventh admission was about four and a half years before the final one, because of marked increase in the severity of her asthma associated with the production of blood-tinged sputum. There were signs of consolidation at the left base and culture of the sputum grew Type 1 pneumococcus. She recovered uneventfully without the aid of serum or chemotherapy. At that time the spleen was again palpated and the liver edge was felt 2 cm. below the costal margin. After discharge she continued to have asthma but was able to control her symptoms by means of adrenalin and aminophyllin. Four months before her final entry to this hospital she was admitted to another hospital, where an acutely inflamed appendix was removed. At the same operation a uterine dilatation and curettage, a bilateral salpingectomy and a left oophorectomy were performed. Following the operation the patient was well, except for profuse vaginal discharge, until three days before entry, when she felt as if she had the "grippe." She became so cold and chilly that she had to use hot water bottles and extra blankets. There was a feeling of "feverishness in the inside." She lost her appetite and developed headache, pain in the back of the neck and pain across the lumbar region of the back. One day before admission she became confused and irrational. Although her asthma had decreased markedly during the day or two preceding entry, seven empty aminophyllin ampules were found near the bed the night before admission. About 2:00 a.m. of the day of admission she became rigid and opisthotonic, and then "shook all over" and frothed slightly at the mouth. The attack lasted about five minutes, during which time she was completely unconscious. Her physician, who arrived forty-five minutes later, gave her 1 cat unit of digitalis intramuscularly to "slow the heart, which was beating 130 to 140 per minute." Later that day she became more stuporous and irrational. A second physician was called, who sent her to the hospital.

Physical examination showed a well-developed and well-nourished woman breathing in a rapid and labored fashion. She was somewhat lethargic and would not answer questions except with "yes" and "no." The tongue was moderately dry. There was moderate resistance to flexion of the neck, and she was unable to place her chin on the chest. The lungs were resonant, and the breath sounds coarse and rough throughout, with a few wheezes. There was generalized tenderness to deep palpation of the abdomen, and bilateral costovertebral angle tenderness. An irregular ecchymotic area was present on the radial aspect of the right index finger. The biceps, triceps, radial, knee and ankle jerks were equal and active. The Babinski, Chaddock, Gordon and Oppenheim tests were positive on the left, with unsustained ankle clonus and a doubtful Kernig sign; all were equivocal on the right.

The red-cell count was 3,580,000, with a hemoglobin of 11 gm. The white-cell count was 13,200, with 80 per cent neutrophils; on smear, there was marked shift to the left, and toxic granulation of the neutrophils. The urine was acid with a + test for albumin and for acetone; the sediment contained 5 to 6 white cells per high-power field and innumerable red cells and granular and cellular casts. Lumbar puncture gave an initial pressure of 165 mm. and a final pressure of 120 mm. after 10 cc. of fluid had been withdrawn. The spinal fluid was faintly cloudy and contained 20 polymorphonuclears, 50 lymphocytes and 830 fresh red cells per cubic millimeter; many intracellular and extracellular gram-negative biscuit-shaped diplococci were seen in the smear, but culture on various mediums gave no growth. Spinal-fluid Wassermann and Hinton tests were negative; the protein was 33 mg., and the sugar 53 mg. per 100 cc. A blood culture taken on the

*On leave of absence.

day of admission was reported positive for *Staphylococcus aureus* (coagulase positive) in both flasks. A blood Hinton test was negative.

Half an hour after admission the patient was given 5 gm. of sodium sulfadiazine in 500 cc. of saline intravenously. The following day the neck was less stiff, the headache was less and she was more responsive although still quite restless. Respirations were labored, and the lungs were full of rhonchi and wheezes. She was given intravenous fluids and 2 ampules of aminophyllin without much apparent improvement. The sulfadiazine level on that day was 13 mg. per 100 cc.; the nonprotein nitrogen, 37 mg. per 100 cc.; the chloride, 88.3 milliequiv. per liter; the carbon dioxide combining power, 20.1 millimols per liter; the protein, 6.5 gm. per 100 cc.

On the second hospital day, three successive white-cell counts were 4700, 3800 and 3700 respectively, with 93 per cent toxic-appearing neutrophils. The sulfadiazine was stopped. The following day the temperature was 100.4°F, and the white-cell count 3500. An x-ray film of the chest, taken with a portable machine on the fourth day, showed mottled increased density at the right base that seemed to be less than it was at the time of examination a year previously. The lung markings were prominent throughout the chest, which was quite emphysematous. The right costophrenic angle was obliterated. No evidence of abscess or bronchiectasis could be demonstrated.

The temperature on the following day rose to 104.4°F. The patient complained of severe headache and pain in the left shoulder and right hip. The ecchymotic area on the right forefinger had broken down, with discharge of reddish-brown purulent material. Similar bluish-black ecchymotic areas were found on the tip of the fifth finger, the sole of the left foot and the right heel. A large area of swelling, exquisite tenderness and redness appeared on the right buttock, near the site of an intramuscular injection of paraldehyde, from which colon bacilli, hemolytic *Staph. aureus* (coagulase positive) and alpha-hemolytic streptococci were cultured subsequently. There was a profuse, greenish, creamy, vaginal discharge, in which many gram-positive cocci in small clumps were seen on the smear. A lumbar puncture gave a clear fluid containing 29 red cells, 2 polymorphonuclear cells and 5 lymphocytes per cubic millimeter. The initial pressure was 275 mm.; the final pressure, 100 mm. The spinal-fluid protein was 31 mg. per 100 cc., and the sugar 64 mg.; culture again yielded no growth. The temperature remained between 102 and 104.5°F. Two other blood cultures were reported positive for hemolytic *Staph. aureus* (coagulase positive). The white-cell count rose to 10,600 on the sixth hospital day.

The patient received 4 gm. of sulfadiazine on the seventh and eighth hospital days and then continued on daily doses of 6 gm. of sulfathiazole. She complained of severe pain in the left anterior chest, where a loud grating pleuritic friction rub could be heard. There was no cough or hemoptysis. The white-cell count was 11,500; the urine showed a ++ test for albumin and contained numerous white and red cells.

On the ninth day many petechiae were noted on the flexor surfaces of the hands and feet, on the conjunctivas and in the buccal mucosa. On the eleventh hospital day the patient's condition was essentially the same. The sulfathiazole level was 13.4 mg. per 100 cc., and the nonprotein nitrogen 52 mg. The blood culture was still positive for hemolytic *Staph. aureus* (coagulase positive). The white-cell count was 12,300. The temperature ranged between 101 and 104°F. The urine showed a ++ test for albumin and a ++++ test for diazine crystals.

On the twelfth day the patient had a convulsion. The sulfathiazole level was 15.2 mg., and the nonprotein nitrogen 120 mg. per 100 cc. The carbon dioxide combining power was 23.2 millimols, and the chloride 74.5 milliequiv. per liter. The white-cell count was 13,500, and the hemoglobin 9 gm. per 100 cc. The spleen was felt for the first time since admission. The sulfathiazole was stopped, and the patient was given 20,000 units of penicillin intravenously, followed by two similar doses in the next four hours and then 10,000 units every two hours for the next two days. Her condition remained about the same. On the fifteenth day she had repeated convulsions and became comatose. The sputum was bloody. There was considerable breakdown of the tissue over the back, the buttocks and the right heel.

An x-ray film of the chest showed a few small linear areas of increased density just behind and above the left diaphragm. No frank areas of consolidation or evidence of pleural effusion or empyema could be seen. A lumbar puncture revealed an initial pressure of 85 mm. The fluid contained 600 red cells, 130 polymorphonuclear cells and 6 lymphocytes per cubic millimeter; no microorganisms were seen in the smear. The blood culture was still positive. The patient received three transfusions of 500 cc. of blood in the following three days and considerable intravenous fluid. The urinary output, however, became very low, and she developed diarrhea. The temperature ranged between 103 and 105°F., the pulse above 100, and the respirations about 40; the blood pressure was 70 systolic, 10 diastolic. The white-

cell count was 17,000, with 84 per cent neutrophils. Injections of 25 per cent glucose in saline were given intravenously, with no apparent effect on the output of urine.

On the nineteenth hospital day the patient's condition appeared worse. She developed anasarca. The left arm was slightly stiff; the left biceps and triceps reflexes were present, but no other reflexes could be elicited. The temperature was 104°F. She was given 40,000 units of penicillin every two hours for five doses without any apparent benefit, and died on the twentieth hospital day.

Differential Diagnosis

Dr. John Norcross*: I think it is fair to say that it is not easily possible to connect all the conditions in this case under one diagnosis. I am going to say that the first part of the story is not connected with the second; that is, the long history of asthma and the violent abdominal pain and palpable spleen recorded at one admission are not related to the events that occurred in the last admission. What caused the abdominal episode, I do not know. We are not given much detail about it and I do not believe, from the point of view of the final episode, that it is important. Four and a half years previously she had had pneumonia, and at that time the spleen was again palpable. I assume from the history that it was then no longer palpable until the final admission.

I think we might date the present illness from four months before the final entry. She continued to have asthma, but at that time she was taken to another hospital where an acutely inflamed appendix was removed. At the same time a uterine dilatation and curettage was done and some of the pelvic organs removed. I think we can safely say that she had a profuse vaginal discharge shortly after this operation, and probably before it also, and since her tubes and one ovary were removed, she may well have had chronic pelvic inflammatory disease, for which this operation really was done. Regarding the appendix, it may or may not have been acutely inflamed.

Two days before entry the patient became acutely ill with fever, chills and rapidly developing signs of meningismus and meningitis. We are told that seven empty ampules of aminophyllin were found near the bed. I have never seen a patient who received the contents of seven aminophyllin ampules in a short course of time; that might cause a convulsion, but I doubt it. In any case I do not believe that it is important from the point of view of the final diagnosis.

At the time of entry to the hospital she was found to be stuporous and had signs that were consistent with meningeal irritation. She also had an ecchymotic area on the right index finger, and positive Babinski and related signs on one side, which are perhaps unusual at this time in the course of meningitis but not at all impossible. She had some degree of anemia, a slight leukocytosis and, what is more important, a marked shift to the left, with toxic granulations in the polymorphonuclear leukocytes.

The urine was abnormal but we do not know whether it was a catheterized specimen. Since she had a profuse vaginal discharge, some of the white cells may have come from the vagina, but the changes were primarily due to disease of the urinary tract. The cellular findings and the granular and cellular casts all signify serious irritation of the kidneys.

The lumbar puncture gave an initial spinal-fluid pressure of 165 mm., and a final pressure of 120 mm. I wonder if the initial pressure could have been higher. The fluid was faintly cloudy, and the cell count showed only a few polymorphonuclear cells, 50 lymphocytes and 820 fresh red cells. Regarding the red cells, I should like to know whether they were present in the early part or at the end of the tap; they may have been the result of difficulty in tapping. "Many intracellular and extracellular gram-negative biscuit-shaped diplococci were seen in the smear." That is the most important finding. They could have been one of two organisms, — gonococci or meningococci, — and I think at this point we should decide which was the more likely. Apparently the service never knew because they were unable to grow them out on a culture medium. The sugar was 53 mg. per 100 cc., which is certainly high for an acute meningitis. A blood culture taken at the same time was reported positive for *Staph. aureus* (coagulase positive). This was repeated several times throughout the rest of the course in the hospital, and we know, therefore, that the patient had a true bacteremia due to a pathogenic staphylococcus. We also know that four months previously the patient had had a radical pelvic operation, presumably associated with an infection in the pelvis, which was likely caused by the gonococcus. Therefore, I am going to venture the guess that this was a gonococcal meningitis.

The patient was given sulfadiazine and responded quite satisfactorily, but they apparently dared not give more because the white-cell count rapidly dropped either because of the toxicity of the condition or because of sensitivity to the drug. We learn later that the clinical symptoms improved and that a second tap done shortly thereafter was negative. No organisms were seen in the smear, and the culture yielded no growth.

*Physician, Lahey Clinic.

The patient then began to take a definite turn for the worse and there were other manifestations, first in the joints, then in the skin and then subcutaneous abscesses. We can therefore say that she had a definite bacteremia, and we have adequate proof from the blood cultures that a pathogenic staphylococcus was the etiologic organism. She then developed pleuritis, further skin manifestations, with petechiae, and additional evidence pointing to trouble with the kidneys. We are told that she had many sulfadiazine crystals in the urine. We also know that at that time the sulfadiazine was changed to sulfathiazole. We wonder, of course, what role these drugs played in the kidney picture. I think we can assume that they played some part, but a minor one. There was evidence of nephritis as the story started, and I think that the later picture was largely a progression of that condition. On the twelfth day she had a convulsion. At that time the nonprotein nitrogen was 120 mg. A lumbar puncture was done shortly thereafter, at which time the spinal fluid contained red cells, polymorphonuclear cells and lymphocytes, but no microorganisms. The blood cultures were still positive. The convulsion might have been caused by the uremia, but I think that it was mostly due to infiltration of the central nervous system by the infection. The urinary output became low, she developed diarrhea and further evidence of uremia, and in spite of the fact that penicillin was given, she rapidly grew weaker and died.

In summary, we have a patient with a picture suggesting gonococcal meningitis, from which she apparently recovered. She then developed evidence of a severe bacteremia, with multiple embolic phenomena of a septic type. There are several possible sources for the bacteremia. The pelvis was the obvious source, and at one point the vaginal smear showed a pathogenic organism that was morphologically identical to that found in the blood culture. I assume that this was the primary source of the organism. The patient also had subcutaneous abscesses, which might have been the source of the bacteremia, but I think that they were secondary rather than primary. The causative organism — a staphylococcus — should have responded better than it did to the sulfonamide drugs, and most certainly to penicillin, unless it was in a place that was difficult to reach, such as the heart valves. The heart is not mentioned in the entire history, and I assume that the physical findings were negative. Nevertheless, that is often true in acute bacterial endocarditis, and it seems to me that the most likely diagnosis is, in addition to the gonococcal meningitis, an acute bacterial endocarditis, due to *Staph. aureus*, the original source having been in the pelvis. We know that the patient had bronchial asthma and that she had bacteremia and, terminally, septicemia. I think she also had embolic glomerulonephritis, with sulfadiazine contributing to the kidney failure and uremia. She may have had multiple brain abscesses or one abscess as part of the general process.

Dr. William Beckman: On the ward we were as bewildered as Dr. Norcross was by the presence of gram-negative intracellular organisms in the spinal fluid obtained at first lumbar puncture, but in view of the prevalence of meningitis at that time we assumed that they were meningococci. When the patient did not respond to chemotherapy we abandoned that idea. We were considerably less astute on the ward than Dr. Norcross because we did not combine the previous abdominal operation with the present illness.

Dr. Francis M. Rackemann: This woman had been a patient in the Allergy Clinic for some years. The interesting thing was the method by which she relieved her attacks. She took aminophyllin intravenously two or more times every day for months at a time, and had been giving it to herself. Her husband also learned how to administer it. When I was asked to see her, my first thought was that she was responsible for the septicemia, because she often told me that she carried her syringe loose and "naked" in her handbag along with her handkerchief and other things and that if she was caught with an attack when she was downtown on a shopping tour she did not bother to wash or clean it in any way, but used it as it was to give herself an intravenous injection. I should like to add that, as is so often the case, the asthma, which was so severe and so persistent, having occurred daily for some years, cleared entirely during the infectious period.

Clinical Diagnoses

Septicemia (*Staph. aureus*).
Acute bacterial endocarditis (*Staph. aureus*).

Dr. Norcross's Diagnoses

Acute bacterial endocarditis (*Staph. aureus*).
Bacteremia and septicemia (*Staph. aureus*).
Embolic glomerulonephritis.
Uremia.
Brain abscesses?
Gonococcal meningitis, healed.
Bronchial asthma.

Anatomical Diagnoses

Pelvic abscess, with extension to right buttock.
Septicemia (*Staph. aureus*).
Acute bacterial endocarditis, mitral valve (*Staph. aureus*).
Septic infarcts of brain, meninges, lung, kidney and spleen.
Subcutaneous abscesses.
(Bronchial asthma.)

Pathological Discussion

Dr. Benjamin Castleman: Of course, the most interesting feature of this case was to discover the source of the obvious staphylococcal septicemia. We found a bacterial endocarditis on the mitral valve—a large, friable, shaggy vegetation, 2 by 2 by 1 cm., attached to one of the leaflets, without any underlying old disease of the valve. This indicates that the lesion was acute rather than subacute, the latter usually developing on a previously damaged valve. On microscopic examination the vegetation was filled with staphylococci.

There was a very large abscess in the right pelvis; it was intraperitoneal and extended down to the obturator foramen, connecting with a large sloughing ulcerating infection on the right buttock. Both tubes had been partially removed. The ovaries were still present and did not appear to be infected. The fundus of the uterus contained a great deal of friable material, and this proved to be inflammatory. Since there was no extension through the wall of the uterus, I do not believe that the uterus was the primary source. I am still not sure whether the abscess was the residuum of an acute appendicitis or of acute pelvic inflammatory disease, and I do not know how one can tell. The abscess was tremendous. The fact that it was on the right rather than bilateral is a bit in favor of its having been due to appendicitis. The organism was the staphylococcus rather than the colon bacillus, which is the usual finding in abscesses following appendicitis, but during the long period following operation the staphylococcus might have overgrown the colon bacillus. There were subcutaneous abscesses throughout the body. The spleen weighed 1030 gm. and contained numerous septic infarcts, which had broken down and formed abscesses. A few small infarcts were present in the kidneys, and numerous abscesses of all ages were found in the lung. There was no embolic glomerulonephritis, and no evidence of sulfonamide changes in the kidneys.

Dr. Kubik will tell us about the brain.

Dr. Charles S. Kubik: The brain showed numerous septic infarcts and several small abscesses, one of which was about 1.5 cm. in diameter. I should like to ask about the biscuit-shaped organisms found in the spinal fluid.

Dr. Beckman: The fluid was examined by several extremely reliable people; but, of course, it is possible that they were overdecolorized staphylococci.

Dr. Kubik: I should say that the meningeal symptoms were almost surely related to the bacterial endocarditis. There were patches of subarachnoid exudate, such as are frequently observed in subacute or acute bacterial endocarditis; these usually result from septic emboli to meningeal vessels rather than from septic infarcts within the brain substance.

CASE 29372

Presentation of Case

First admission. A fifty-one-year-old housewife was admitted to the hospital because of swelling of the abdomen and jaundice of several weeks' duration.

Twenty-eight months before admission, she developed "grippe," with fever of 104°F., weakness, anorexia and malaise. The abdomen was enlarged. There were jaundice and right epigastric pain. She was admitted to a community hospital where, following x-ray examinations, she was told that she had three tumors but that she was too weak to be operated on. She was discharged home under the care of a practical nurse. During the next seven months she was bedridden, and although she lost 15 pounds of weight, she gradually gained strength and resumed her household activity for the next eighteen months. The jaundice had apparently disappeared. At that time, that is, three months before admission, she fell, striking the chest and right side of the abdomen. Five days later she had a swelling of the right knee, which persisted for several days. The vague pain in the right upper quadrant returned. One month before entry she developed a "cold" and coincidentally became jaundiced. The urine became dark, but no change in the character or color of the stools was noted. Three weeks before admission her abdomen and feet began to swell and steadily became larger. During one week she had nocturia (three or four times). Her appetite had been poor for the three weeks preceding entry, but there had been no nausea or vomiting.

Five years before admission, following her husband's death, the patient began drinking hard liquor—mostly gin—rather heavily and "stopped eating."

Physical examination showed deep jaundice of the skin and scleras. Numerous telangiectases were present on the face and neck, and there were many dilated superficial veins over the abdomen. A few dry rales were heard at the right base. The abdomen was large and tense, and the umbilicus

was everted. There was a definite fluid wave, with bulging flanks. The liver was easily ballotable 11 cm. below the costal margin in the midclavicular line; the edge was vaguely irregular and could also be felt on the left side of the abdomen. The spleen was palpable 4 cm. below the left costal margin. There was moderate pitting edema of the feet and lower legs. The ankle and knee jerks were absent.

The blood pressure was 140 systolic, 80 diastolic. The temperature was 99.3°F., the pulse 104, and the respirations 19.

The urine was brown, had a specific gravity of 1.018 and gave a ++++ test for bile. Examination of the blood showed a red-cell count of 3,250,000, with a hemoglobin of 70 per cent. The white-cell count was 14,900, with 62 per cent neutrophils. The stools were brown, mushy and guaiac negative. The blood protein was 8.9 gm. per 100 cc., the albumin being 3.4 gm. and the globulin 5.5 gm., making an albumin-globulin ratio of 0.6; the van den Bergh test was 13.1 mg. direct and 19.6 mg. indirect. The prothrombin time was 38 seconds (normal, 18 seconds). The hematocrit was 40. A blood Hinton test was negative.

On the second hospital day a paracentesis yielded 5000 cc. of clear bile-colored fluid with a total protein of 1.7 gm. per 100 cc. No sediment could be obtained. Culture gave no growth. Palpation of the abdomen then revealed a firm, nodular, irregular, tender liver extending across the upper abdomen down to 3 cm. above the umbilicus. The spleen was palpable four fingerbreadths below the costal margin. The patient was placed on a high-vitamin, high-carbohydrate diet. X-ray examination on the sixth hospital day showed a high diaphragm on both sides, a small amount of fluid in both pleural cavities and a transverse position of the heart.

The patient was now given 1 ampule of Hykinone daily. During the first ten days she was weak, drowsy and nauseated. The pulse was elevated. Later, however, her general condition improved appreciably. On the fifteenth hospital day the temperature and respirations were about normal, and the pulse 90 to 100. The blood protein was 5.6 gm. per 100 cc., the albumin being 3.4 gm. and the globulin 2.2 gm., making an albumin-globulin ratio of 1.6. The van den Bergh test and the prothrombin time were unchanged. A cephalin-flocculation test on the blood was ++++ in twenty-four and forty-eight hours. The urine gave a ++ test for albumin and a ++++ test for bile. The white-cell count was 12,700.

One month after admission the pulse ranged between 90 and 70, and the temperature between 98 and 100°F. The blood protein was 7.5 gm. per 100 cc., the albumin being 2.8 gm. and the globulin 4.7 gm., making an albumin-globulin ratio of 0.6. The blood bilirubin, according to the van den Bergh test, was slightly lower. The patient was transfused. A second paracentesis during the fifth hospital week gave 5000 cc. of similar fluid. The liver was then palpable 7 cm. below the costal border at the midclavicular line. The temperature and respirations were normal, and the pulse ranged between 60 and 100. She was discharged to a nursing home.

Final admission (nine days later). Following discharge the patient did fairly well until four days prior to re-admission, when she developed chilly sensations, irritating cough productive of small quantities of greenish sputum and a temperature of 102°F. The following day, during a bout of coughing, she suddenly felt weak, dizzy and slightly nauseated. There was some desire to move the bowels. Two days prior to re-admission she vomited black, foul-tasting "blood" on two occasions; no bright blood was seen. The day before entry she had frequent, loose, tarry stools.

Physical examination was essentially the same as before. There was no peripheral or sacral edema.

The blood pressure was 130 systolic, 55 diastolic. The temperature was 100°F., the pulse 20, and the respirations 30.

The red-cell count was 2,700,000, with a hemoglobin of 7 gm. The stools gave a ++++ guaiac test.

During the next two days, she had several "currant jelly" stools. She became disoriented and delirious, and died on the third hospital day.

Differential Diagnosis

Dr. Wyman Richardson: The moral of this case perhaps is, If you let demon rum get after you too much, be sure to eat enough. The interpretation of drinking "rather heavily" differs with each patient but when associated with the remark that she "stopped eating," it probably means a good deal more drinking, rather than less.

To go back to the history a moment, the question is, Did the illness begin with the febrile episode twenty-eight months before admission? It is stated that the abdomen was enlarged. If that means enlargement due to ascites, this suggests that her illness began before the febrile illness; if it was just fat, maybe not. I suspect, however, that her illness began before the febrile episode. I shall disregard the three tumors.

The patient then entered this hospital with evidence of something wrong in the liver. Physical examination revealed a big liver, which, by some observers, was thought to be nodular. It is diffi-

cult to be sure about a nodular liver. Certainly one cannot feel a hobnail on a liver, but sometimes when there is tumor or the hepar-lobatum type of syphilis of the liver one can feel what might be called nodules or an irregular liver. It is significant that the spleen was palpable. Whether it is important that the knee jerks were absent, I am not certain.

The laboratory data are consistent with hepatic failure. As we have seen several times, the total protein was elevated, but the elevation was due to increase in globulin, often with a decrease in albumin. Just why it changed so quickly between the second and third determinations, I do not know.

The blood picture, so far as we are given it, is not suggestive of the ordinary type of pyogenic infection. We are told that the stools were brown; in other words, she was putting out some bile. The anemia appears to have been of the macrocytic type, since, according to the hematocrit of 40, the volume of the cells must have measured over 100 cubic microns. I should like to point out that each time the patient had a febrile episode, she seemed to get worse, until the final admission when she had sudden weakness, dizziness and nausea, obviously associated with hemorrhage. The bleeding in this case appears to have been massive and rather more than one would expect simply from the lack of prothrombin. In other words it suggests that there were varicose veins and that she ruptured such a vessel.

So we have a patient with hepatic failure, a big liver and a history of alcoholism. The diagnosis that I think most nearly fits the situation is a toxic cirrhosis and hepatitis, probably alcoholic. There is abundant experimental evidence in animals that substances that are toxic for the liver can be controlled to a considerable extent by dietary measures or the use of substances derived from food. It is also suggested that the people who get into liver trouble from drinking are deficient in their diets in some respect.

There are other conditions that have to be seriously considered. First, I shall mention the question of tumor. The bugbear of hepatoma always comes in, and usually one is wrong, because it is a relatively rare tumor. The cases of hepatoma that I have seen or discussed here have had a more clear-cut story of an antecedent portal type of cirrhosis of rather long standing. Furthermore, the presence of an enlarged spleen may be taken as evidence against other types of neoplasm, although one cannot be sure of that. There is nothing to suggest tumor except the original observation that there were three tumors. Just how they were discovered, whether by x-ray or physical examination, is not clear. In general the story to me is perfectly easily explained on the basis of hepatic failure. The increase in the amount of failure associated with the febrile episodes is probably that commonly seen with ordinary respiratory or other epidemic infection. I am going to rule out tumor.

Another consideration that we always have to think of is syphilis. We regularly get caught on syphilis of the liver, in some cases by laying too much stress on a negative Hinton test that was not done in dilutions and in others by not paying enough attention to a positive Hinton test. This patient had a negative test. The absence of knee jerks does not necessarily mean that she had syphilis. I cannot be sure that she did not have syphilis of the liver, but I do not see anything in favor of it.

Finally, can this be subacute yellow atrophy in which regeneration had been going on for a long time? In such cases the liver may be enlarged, but I doubt that it would be as big as this one was.

To summarize, I should call this a toxic hepatitis and cirrhosis of the liver — probably alcoholic. I think the patient had varices, and probably died of hemorrhage from varices, although there can be a considerable amount of hemorrhage without one's being able to discover the source. I might add one thing. It is not too uncommon to find a peptic ulcer in association with cirrhosis of the liver. Possibly I ought to throw that in so as not to get caught, but I shall say that the hemorrhage was from varices, even though they were not demonstrated by x-ray study. So much for the liver.

The patient had a chill, fever and greenish sputum, and she may have had some pulmonary infection terminally.

DR. BENJAMIN CASTLEMAN: There was an x-ray film of the esophagus.

DR. MILFORD SCHULZ: I cannot be sure that there are any esophageal varices in this film.

DR. WILLIAM BREED: Is there no way, except by guessing, to determine the presence or absence of hepatoma on superimposed cirrhosis?

DR. SCHULZ: Sometimes a hepatoma projects through the diaphragm, forming a bulge in the upper part.

DR. CASTLEMAN: Is it not true that these patients have fever and signs of malignant disease?

DR. RICHARDSON: Not necessarily, but I think one might get a hint in the blood picture if there were widespread bone-marrow involvement.

DR. ROBERT KINNEY: Is it not worth while to examine the ascitic fluid for tumor cells?

DR. CASTLEMAN: Unless there is widespread seeding, which is extremely unusual in hepatoma, it is difficult to find tumor cells in the ascitic fluid.

DR. JACOB LERMAN: We thought that the diagnosis was alcoholic cirrhosis and that she had, in

addition, a superimposed toxic hepatitis. We also believed that hepatoma was not likely because of the relatively short duration and the rapid onset of jaundice.

Clinical Diagnoses

Alcoholic cirrhosis of liver.
Toxic hepatitis.
Bleeding from esophageal varices.

Dr. Richardson's Diagnoses

Toxic hepatitis.
Cirrhosis of liver, probably alcoholic.
Hemorrhage from varices.
Pulmonary infection (terminal)?

Anatomical Diagnoses

Cirrhosis of liver, alcoholic type.
Acute hepatitis, severe.
Gastrointestinal hemorrhage from gastric varix.
Jaundice.
Ascites.
Splenomegaly.
Bronchopneumonia.
Leiomyoma of uterus.

Pathological Discussion

Dr. Castleman: At autopsy this patient had a large liver, which weighed 2500 gm. It was hard and green. Ordinarily, a hard, green liver immediately makes one think of biliary obstructive cirrhosis. Examination of the biliary tract, however, showed that it was perfectly normal; there was no obstruction. The granularity of the liver was that ordinarily seen in alcoholic cirrhosis. The nodules were uniformly minute, in contrast to the toxic or healed acute-yellow-atrophy type of cirrhosis, in which the nodules vary in size. The liver of alcoholic cirrhosis is usually yellowish brown, not green; however, microscopic sections showed why it was green — a marked acute hepatitis was superimposed on the alcoholic cirrhosis. The liver cells were granular and necrotic, and in many places had disappeared. The spleen was also enlarged, weighing 420 gm. The uterus contained a huge fibroid; hence, the patient did have three tumors — an enlarged liver, an enlarged spleen and an enlarged fibroid uterus.

The cause of exitus was hemorrhage into the gastrointestinal tract, but not from esophageal varices. The submucosal esophageal veins were not prominent. However, in the stomach, 4 cm. proximal to the pylorus, we found a small papilla 4 mm. long and 2 mm. in diameter, which on microscopic examination proved to be a thrombosed varix. This had ruptured and was the source of the gastrointestinal hemorrhage, rather than rupture of a vessel at the base of a peptic ulcer. Close by was a small erosion without the fibrinoid change characteristic of peptic ulceration. There were two small varices beneath this erosion, and I believe that pressure of the larger varix, plus perhaps the impaired vascularity due to the two smaller varices, accounted for the erosion. There was no gastritis such as one might expect to go along with peptic ulceration.

The patient also had terminal bronchopneumonia.

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BLOOD PLASMA

With the accelerating tempo of the war, the need for blood plasma is constantly increasing. In fact, the demands on the various blood-donor centers of the American Red Cross have become so great that some difficulty in obtaining the required number of donors is being experienced. Just why this is so is difficult to understand, since the total amount of plasma for which any one center is responsible can be obtained from a relatively small percentage of the surrounding population, and certainly the slight sacrifice of time and minor discomfort to the donor are greatly outweighed by the saving of the lives of literally thousands of soldiers and sailors on extended battlefronts.

It has been said that the medical profession has failed to support the program wholeheartedly, and this statement is based chiefly on the fact that many members of a prospective donor group often refuse to give blood, with the excuse that their physicians have advised them against it. Although it is true that a few ultraconservative physicians question the advisability of repeated bleedings on the ground that no one knows the eventual effect, it is difficult to understand how the removal of moderate amounts of blood at adequately spaced intervals in a healthy and active person can do the slightest harm. The healthy professional donor who has given blood for a hundred or more transfusions is no rarity. Furthermore, in those with moderate or severe hypertension or with an excessive amount of blood, as in erythremia, bloodletting at regular periods is an accepted therapeutic procedure. In other words, there seems to be little sound evidence for believing that many of these excuses are founded on fact, but rather are "white lies" prompted by fear and conceived at the moment as the "easiest way out."

In any event, it behooves physicians to support this worthy program to the utmost. Properly couched statements concerning the value and need of plasma, the care taken at the donor centers to weed out persons who should not give blood and the relative safety and minimal annoyance of the blood-taking procedure will do much to reassure those who are hesitant to do their bit toward the saving of a life.

ROCKY MOUNTAIN SPOTTED FEVER

An article published elsewhere in this issue of the *Journal* calls attention to the need for Massachusetts physicians to appreciate that Rocky Mountain spotted fever is endemic in the Cape Cod region. Although no cases have been reported since the summer of 1939, this is no guarantee that the infective agent has been eliminated. In fact, in areas in the West, where the disease is

relatively prevalent, cases in any one endemic area may not be reported for several years, only to recur subsequently.

It is pointed out that although the infective agent may have been introduced within the past decade by a dog carrying infected ticks or by tick-infested rabbits imported from regions where the disease is endemic, it seems more likely that a small number of local dog ticks — the insect vector of the disease to human beings — have harbored the virus for many years. However, the incidence of infection among ticks must be exceedingly low to account for the rarity of the disease.

The paucity of cases certainly does not warrant the widespread use of the specific rickettsial vaccine, but all physicians should bear in mind that any patient with an unexplained maculopapular rash and fever who has visited Cape Cod is likely to be suffering from Rocky Mountain spotted fever. This is particularly true in the case of children who are more likely than adults to have been bitten by ticks. The diagnosis can be established early in the disease by recovering the infective agent from the patient's blood, but the procedure is time consuming. After the first week of the disease, several reliable serologic diagnostic methods — agglutination tests with strains of Proteus (Weil–Felix reaction) or with rickettsial agents or complement-fixation tests — are available, and the latter have been shown to remain positive for several years after an attack of the disease. With these laboratory aids, together with quite characteristic clinical symptoms, diagnosis should not be difficult.

MEDICAL EPONYM

Felty's Syndrome

Augustus Roi Felty (b. 1895), when a junior member of the staff of the Johns Hopkins Hospital, was the author of a paper "Chronic Arthritis in the Adult Associated with Splenomegaly and Leucopenia" in the *Bulletin of the Johns Hopkins Hospital* (**35:** 16–20, 1924):

> The syndrome occurred in individuals of middle age (45-65), the average being 50 years. All the patients gave a history of marked loss of weight since the onset of symptoms. . . . The arthritic process is distinctly chronic. . . . The objective findings both by physical examination and roentgenographic study are neither widespread nor indicative of a very damaging or destructive process. . . .
>
> In every case the spleen was palpably enlarged . . . firm but not tender. . . . In every instance there was noted a yellowish-brown pigmentation of the skin. . . .
>
> In all cases save one there was a slight secondary anemia. . . . Most striking was the leucopenia, which was a distinctive feature in every case. The leucocyte counts varied from 1000 to 4200. . . .
>
> The etiology is entirely obscure, though the various findings seem best accounted for as manifestations of a single disease process.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

O'BRIEN — John F. O'Brien, M.D., of Fall River, died June 11. He was in his fifty-eighth year.

Dr. O'Brien received his degree from McGill University Faculty of Medicine, Montreal, Quebec, Canada, in 1910. He was a member of the Massachusetts Medical Society and the American Medical Association.

SENECAL — Raymond E. Senecal, M.D., of New Bedford, died August 24. He was in his fifty-second year.

Born in St. Cesaire, Canada, Dr. Senecal received his degree from Boston University School of Medicine in 1917. He was on the staffs of St. Luke's Hospital and Union Hospital, New Bedford, and Acushnet Hospital and St. Anne's Hospital, Fall River. Last month he was appointed a member of the Public Health Council by Governor Saltonstall. Dr. Senecal was president of the New Bedford Medical Society at the time of his death. He was a member of the Massachusetts Medical Society, the American Medical Association, the Franco-American Civic League and the Franco-American Historical Society.

His widow, a son and two daughters survive.

STICKNEY — Robert C. Stickney, M.D., of Beverly, died September 7. He was in his forty-ninth year.

Dr. Stickney graduated from Dartmouth College and received his degree from Columbia University College of Physicians and Surgeons, New York, in 1919. He specialized in pediatrics and was a member of the staff of the Beverly Hospital and the North Shore Babies Hospital in Salem. Dr. Stickney had been chairman of the Beverly Board of Health for many years. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and a daughter survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

THE EMERGENCY PROGRAM FOR THE CARE OF WIVES AND INFANTS OF MEN IN THE ARMED FORCES

The Children's Bureau has approved the Massachusetts plan for the emergency care of the wives

and infants of men in certain groups in the armed forces. The funds for the program are provided by the federal government and administered by the Massachusetts Department of Public Health through the Division of Child Hygiene. Payment is made for complete maternity service including prenatal care, delivery in a hospital, postnatal care and pediatric care of the infant until its first birthday. In each case the physician and the hospital agree to accept no additional fees from any other source for the patient during the period when care is authorized for payment by the Massachusetts Department of Public Health.

Eligibility

The wives of men in Grades 4, 5, 6 and 7 of the Army, Navy, Marine Corps and Coast Guard are eligible under this plan. Also included in the group are the wives of Army and Navy aviation cadets. Wives of men who are in Grades 1, 2 and 3 may receive care only if they sign a certificate of need.

Applications

Applications for maternal or infant care must be made by the service man's wife and her physician on a special form provided by the Department of Public Health. This application should be sent immediately to Dr. Florence L. McKay, director, Division of Child Hygiene, 73 Tremont Street, Boston. Application forms are available through the Division of Child Hygiene, state district health officers, local boards of health, prenatal clinics, chapters of the American Red Cross, Army cantonments, Navy stations, visiting-nurse associations, bureaus of the Travelers Aid Society and similar social-service organizations.

Types of Care Provided

Maternal care. The Massachusetts plan provides payment for hospital delivery only. The attending physician may be paid for one of the following:

Prenatal, delivery and post-partum service (the latter includes examination of mother and infant at six weeks). Prenatal visits should include pelvic measurements and, routinely, weight, blood pressure, urinalysis and hemoglobin determinations.
Delivery and post-partum service only.
Prenatal service only.

The physician who gives maternal care sends a report of service rendered on a special form to the Division of Child Hygiene with his bill for services. Payment will be made only on receipt of the bill and the report. If there is a question concerning the care given, the Technical Committee on Obstetrics will act on the case. A minimum of ten days and a maximum of fourteen are allowed in the hospital for ordinary cases. If more time is needed, special authorization must be asked by the physician. Prenatal clinics are to be used for prenatal care where available. If the clinic regularly makes a charge to the patient, the fee may be paid through these funds.

Infant care. Payment for infant care will be made only during the infant's first year of life. Pediatric care consists of two types:

Health supervision, which is limited to one visit per month for supervision or immunization or both.
Care of the sick infant.

The sick infant may be cared for in the home or in the hospital for a period limited to three weeks. Special authorization must be requested if the period is extended beyond this point.

Where local well-child conferences, with at least monthly service, are available, health supervision may be given in the conference and the conference will be paid if it regularly charges a fee.

The physician giving pediatric care sends a report of services rendered in the case on a special form to the Division of Child Hygiene, with his bill for services. Payment will be made only on receipt of the bill and the report.

Nursing care. Only bedside care by nurses licensed or eligible for license in Massachusetts may be furnished under this plan. Prenatal supervisory visits are not included for payment.

The state district health officer receives a copy of each authorization from the Division of Child Hygiene. In this way the public-health nursing supervisor for the district is able to provide adequate prenatal supervisory visits, as well as bedside nursing care for the mother or infant.

Hospital care. Hospital care furnished to mothers or infants is at ward rates only. The hospital must agree to accept no other payment for hospital care from any other source during the period when care is authorized by the Massachusetts Department of Public Health.

Fees for delivery rooms, anesthesia, blood transfusions, unusually expensive drugs, ambulances and so forth are extra items and payment will be made at rates usually charged to ward patients.

Payments Authorized Under This Plan

The attending physician may be paid according to the fee schedule that is appended. Payment for service under this plan is not retroactive. The fees allowed cover only the period after the wife signs the application blank. In emergencies, the application must be sent so as to reach the Division of Child Hygiene within twenty-four hours after the beginning of the emergency. In such cases, authorization for payment may be issued if the request is in accordance with the approved regulations.

The cost of care by the intern and resident staff of a hospital is included in the ward cost, and these

physicians will not be paid for medical service rendered to ward patients. Payment may not be made to an attending physician for service customarily provided to ward patients without reimbursement.

According to the regulations of the Children's Bureau, a fee for any one operation may not exceed the total cost of care; for example, the fee for an obstetric operation cannot be more than $50. The attending physician cannot be paid for an operation; he must call a consultant, who will either operate or designate a specialist to do the operation. A description of the consultant service under this plan will be published at a later date, with a list of the obstetric and pediatric consultants.

Standards of Medical Care

The standards of both maternal and infant care are supervised by technical committees. The standards published in the pamphlet *Prenatal Care*, published by the Children's Bureau must be followed for prenatal care.

The physician who is to be paid for maternal or infant care must be a graduate of a Grade A medical school. Graduates of other medical schools who have had training or experience in obstetrics or pediatrics that is approved by the technical committees may be paid.

Technical Committees

The technical committees are appointed by the Commissioner of Public Health. Each committee comprises six physicians who are diplomates in their special fields.

The personnel of the Technical Committee on Obstetrics is as follows:

Dr. R. L. DeNormandie, Boston
Dr. R. J. Williams, Lynn
Dr. Raymond Titus, Boston
Dr. Louis Phaneuf, Boston
Dr. Judson Smith, Boston
Dr. Thomas Almy, Fall River

The personnel for the Technical Committee on Pediatrics is as follows:

Dr. W. R. Sisson, Boston
Dr. Stewart Clifford, Boston
Dr. Robert Moulton, Salem
Dr. Arthur Kimberly, Worcester
Dr. R. M. Smith, Boston
Dr. James Baty, Brookline

* * *

Fee Schedule*

Medical Fees

Maternity Care:

Complete maternity care (at least five prenatal visits, delivery and post-partum care) $50.00

Delivery and post-partum care only 35.00

Prenatal care only (in physician's office) 15.00

Consultation service:

Office visit 5.00

Hospital visit when consultant is on staff 5.00

Home visit or visit to any other hospital 10.00

Travel — allowance for 25 miles or more at 4½c per mile

Telephone — allowance for long-distance telephone calls

Operations:

Obstetric or nonobstetric operations (maximum) 50.00

Other fees to be set by the Technical Committee on Obstetrics as need arises.

The attending physician cannot be paid for any operation. If obstetric operation is indicated, he should call on a consultant for this service. If nonobstetric surgery or other special treatment is needed, the specialist may be chosen by the consultant who is called on the case.

Infant Care (during first year of life only):

Well infant (medical supervision):

Office of private physician for complete examination at initial visit or immunization, or both, per visit 2.00

At well-child conference, per visit ..... .50

Will be paid only to conferences regularly charging a fee; bills should be sent when the amount reaches $5.00.

Sick infant (diagnosis and medical care):

Initial authorization for care of the sick infant can be given for a period not to exceed three weeks. A request must be made for extension of service.

First visit:

At home (maximum) 3.00

In office or hospital 2.00

Additional visits:

At home 3.00

In office or hospital 2.00

Maximum payment for first week of illness 15.00

Maximum payment for second and third weeks, per week 6.00

Maximum payment beyond third week (after special authorization is given), per week 6.00

Consultation service:

Office visit 5.00

Hospital visit when consultant is on staff 5.00

Home visit or visit to any other hospital 10.00

Travel — allowance for 25 miles or more at 4½c per mile

Telephone — allowance for long-distance telephone calls

Operations (maximum) 50.00

Other fees to be set by the Technical Committee on Pediatrics as need arises.

The attending physician cannot be paid for any operation. If operation is indicated, he should call upon a consultant. When the services of a specialist are required, the consultant will designate the specialist.

Hospital Fees

In accepting the case, the hospital agrees to make no charge to patient and to receive payment from the Massachusetts Department of Public Health at the following per-diem ward rates:

Metropolitan Boston $4.00

Outside Metropolitan Boston 3.50

Delivery room, anesthesia and unusually expensive drugs may be paid for at minimum ward rates.

The cost of blood for transfusions may be paid for at the customary rate of the hospital for ward patients.

Cost of ambulance service may be paid for at the rate of $3 for three miles and 50 cents per mile thereafter.

Maternity cases — minimum stay of ten days, maximum of fourteen days. Extension may be had when necessary with special authorization.

Sick infant — maximum allowance of three weeks on initial authorization. Extension may be had when necessary with special authorization.

Where the prenatal clinic regularly charges a fee, $1.50 per visit will be allowed for prenatal care.

In an emergency, when the patient must enter a hospital without authorization, application for payment for services must be made to the Division of Child Hygiene, Massachusetts Department of Public Health, within twenty-four hours.

*The bill for service and the report of each case are to be submitted on the letterhead of the physician, hospital or nursing organization to the Division of Child Hygiene, Massachusetts Department of Public Health, 73 Tremont Street, Boston, immediately after service is given.

Nursing Fees	
Post-partum visits, per visit	$1.25
Home delivery (maximum)	10.00
Home visit for sick infant	1.25

CANCER SYMPOSIUM

In connection with the wartime conference of the American Public Health Association, to be held at the Hotel Pennsylvania in New York City, a one-day cancer symposium will be held on October 11. The participants comprise the heads of the cancer programs in thirteen states and representatives of the American Society for the Control of Cancer and the National Cancer Institute, as well as several outstanding surgeons and educators. The morning session will be devoted to a discussion of the epidemiology of cancer. At a luncheon session ($2.25), to be held at the Hotel McAlpin, administration will be discussed. Service to cancer patients will be the subject for the afternoon session, and education in cancer, that of the evening session.

A general invitation to attend the symposium is extended to all Massachusetts physicians. Those who are interested are requested to notify the Massachusetts Department of Public Health, Room 546, State House, Boston.

MISCELLANY

COLLEGE CAMPUSES IN FIGHT AGAINST TUBERCULOSIS

Out of 860 colleges and universities that received the annual survey questionnaire of the Tuberculosis Committee of the American Student Health Association, 488 replied and 311 reported tuberculosis case-finding programs in operation. In view of the heavy losses in student-health personnel and other serious disturbances experienced by many schools because of the war, this report represents encouraging progress in tuberculosis control among institutions of higher education. It is significant that colleges with a definite control program discovered new cases of pulmonary tuberculosis almost eighteen times as frequently as did those colleges with no program. The following paragraphs are abstracted from a recent article (Lees, H. D. Tuberculosis among college students. *Journal-Lancet* **63**:98–101, 1943) covering this subject.

The twelfth annual report of the Tuberculosis Committee of the American Student Health Association gives striking proof of the value of a tuberculosis control program as a regular part of student health service. In the 311 progressive colleges and universities (total student enrollment, 558,075) reporting such programs, 744 new cases of tuberculosis were discovered, a rate of 133.5 new cases per 100,000 students. At 177 colleges (total student enrollment, 146,000) which provided no such programs, 11 new cases came to light, a rate of 7.5 per 100,000 students. Twenty-two food handlers were found to have pulmonary tuberculosis, and among faculty and other administrative officers, 40 new cases were discovered, thus bringing the total of new cases found in colleges during the school year 1941–1942 to 817.

Few diseases impose such costly and far-reaching penalties for public or personal failure to provide early diagnosis as does tuberculosis; yet the majority of institutions of higher education in this country still fail to employ modern tuberculosis case-finding methods, which are simple and not expensive. The years of disability and suffering and the financial costs involved will reach staggering proportions, and there will be numerous deaths whenever we neglect early diagnosis of tuberculosis.

It is estimated that the complete cost of finding an undiscovered case of tuberculosis among college students on now unprotected campuses might run as high as $166. This may seem expensive to some, who do not take into account the social and economic values involved in the early diagnosis of the disease. Failure to provide modern case-finding programs, however, will invariably prove far more costly to unfortunate individuals, families and communities, and can never redound to the credit of a negligent institution.

Table 1. *Testing Technics in 254 Colleges Reporting Tuberculin-Testing Programs (1941–1942).*

Data	No. of Colleges
Testing method:	
Mantoux intradermal test	182
Vollmer patch test	54
Pirquet test	4
Combined Mantoux and patch test	3
Unspecified	11
Testing material:	
Purified protein derivative	93
Old tuberculin	89
Combination of the two	1
Testing dosage:	
Two-dose technic	63
Single large dose	35
Single intermediate dose	37
Single small dose	37
Combination of doses	2
Testing routine:	
New students and all negative reactors annually	63
New students only (no retesting)	49
New students and all seniors	29
Test optional (available to all annually)	47
Other testing routines	46

The tuberculin test provides the most sensitive and reliable index of the prevalence of tuberculous infection. In the young adult group, for the country as a whole, 21.8 per cent of students react to tuberculin, the East Coast and West Coast sections having a higher infection rate than other sections of the country.

Many of the older, largely exploded, ideas relating to tuberculosis seem still to be firmly lodged in the minds of many people. The belief is all too prevalent that early tuberculosis gives rise to early symptoms. Certain institutions report various procedures for the follow-up of "suspects." "Weighing at frequent intervals" and "frequent temperature readings" are among the commoner of these. The suspects are usually those students who are markedly underweight. The committee therefore feels justified in emphasizing again the fact that the tuberculin test and the chest x-ray provide the only adequate means for the early detection of presymptomatic tuberculosis in the vast majority of cases.

Although it is not possible to speak in exact terms

of the incidence of tuberculosis as applying to the country's student population, reports available to the committee seem to indicate a decline of approximately 30 per cent in its prevalence among college students during the past six years. This may be on the conservative side, for during this period reports from many of the larger institutions conducting excellent case-finding programs indicate an extension of these procedures to include a higher percentage of their students. It is evident that more students are being examined each year and that the technics employed have improved and become more effective.

That there are various technics used in tuberculin testing is shown in Table 1. The Mantoux intradermal method continues to lead all others, while P.P.D. and O.T. are fairly even choices in testing materials. A comparatively large number of colleges use the two-dose technic.

Table 2. *X-Ray Procedures Reported by Various Institutions (1941–1942).*

Data	No. of Colleges
Colleges reporting tuberculin-testing program (254):	
Positive reactors x-rayed once	74
Positive reactors x-rayed annually	66
X-ray optional (acceptance general)	60
X-ray optional (acceptance not satisfactory)	10
Other x-ray routines	19
Fluoroscope used routinely to supplement x-ray	38
Fluoroscope used exclusively (chest x-ray when indicated)	12
Colleges reporting no tuberculin-testing program (57):	
Chest x-ray for all new students	22
Chest x-ray for all students annually	9
Other routine x-ray programs	26

Sixty-six colleges report the ideal annual x-ray of positive reactors. The various x-ray procedures reported are indicated in Table 2.

During the school year 1942–1943 the committee enlisted the co-operation of a group of eastern colleges in a study of entering students approximating 10,000 in number. Information concerning each student includes age, home address, name and location of secondary school attended and whether a private, public or parochial school; tuberculin test technic and results; and x-ray findings. It is hoped that this survey may continue without interruption for a period of ten years or longer, thus providing data indicating differences in the prevalence of tuberculous infection among students from various states and various home communities, accurate yearly comparisons, as well as supplying an index of any changes in the prevalence of tuberculous infection among students in any area.—Reprinted from *Tuberculosis Abstracts* (September, 1943).

CORRESPONDENCE

ESSENTIAL PHYSICIANS

To the Editor: Many doctors regarded as essential—though not of necessity permanently essential—to the needs of Massachusetts have recently received letters asking them to apply for commissions and to have physical examinations. The letters which they have received emphasized that no essential man will receive a commission until he has been declared available by the Procurement and Assignment Service, and the latter has been ordered by the War Manpower Commission to declare no essential man available until a satisfactory replacement for him is found.

It is clear that as the war lasts, medical officers are likely to be invalided out from the Army and Navy, and will filter back into civilian practice. It is anticipated that many such physicians, as they return, will be able to resume the positions that they held previously in the various communities, and that as they return they may be able to take the place of men now called essential, who will thus become available for military service.

It should be re-emphasized that essential men who now apply for commissions will not receive them until they have been declared available to do so by the Procurement and Assignment Service, and that Procurement and Assignment has been directed by the War Manpower Commission to declare no such men available until, in fact, satisfactory replacement for them can be found.

Reginald Fitz, M.D., *Chairman*
Massachusetts State Committee
Procurement and Assignment Service
319 Longwood Avenue
Boston 15

BOOK REVIEW

Psychoanalytical Method and the Doctrine of Freud. By Roland Dalbiez. With an introduction by E. B. Strauss, M.D. (Oxford), F.R.C.P. Translated from the French by T. F. Lindsay. 8°, cloth, Vol. 1, 415 pp. and Vol. 2, 331 pp. London: Longmans, Green and Company, 1941. $9.00.

These two volumes, one of which is entitled "Exposition," and the other, "Discussion," are far too technical for an extended notice in this journal. Both the original French edition and the English translation have already been critically reviewed in psychiatric and psychoanalytic journals.

The general introduction by Dr. E. B. Strauss emphasizes that Freud's claim to enduring fame in the history of thought is securely established. The purpose of the author is to point out that the writings of Freud contain two serious defects. In the first place, Freud makes no clear distinction between his method and his doctrine, and secondly, the author claims that Freud is incapable of presenting his thought in a convincing form. Because of these alleged defects an attempt is made to give an objective statement of psychoanalysis.

The first volume discusses the psychopathology of everyday life, dreams, the sexual theory, the general theory of the neuroses and psychoses, the structure of the mental apparatus and the cultural applications of psychoanalysis. In the second volume, there is discussed at length the unconscious, the theories of sex and psychic causality. In both these volumes the author states that he is neither for nor against psychoanalysis, his purpose being, on the contrary, to distill from the psychoanalysis of today the results that will remain part of the science of tomorrow. His approach can, perhaps, be best summarized in his own words: "I believe that the metaphysical system which would most logically extend the results which Freud has reached, would, on the whole, be of the Aristotlean type."

(Notices on page x)

Foresight in Surgery

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NOTICES

FIFTIETH ANNIVERSARY OF TUFTS COLLEGE MEDICAL SCHOOL

A notice of the exercises to be held at the fiftieth anniversary of Tufts College Medical School appeared in the September 9 issue of the *New England Journal of Medicine*. The following changes have been made:

September 22: 12:00 noon, at Tufts College Medical School. Colonel Raymond W. Bliss, assistant to the Surgeon General of the United States Army, will speak on the topic, "Plans and Operations of the Surgeon General's Office."

September 29: 4:00 p.m., at Tufts College Medical School. There will be an unveiling of portraits of Dr. Leary, professor of pathology emeritus, and Dr. Cadis Phipps, professor of medicine.

SUFFOLK CENSORS' MEETING

The censors of the Suffolk District Medical Society will meet for the examination of candidates at the Boston Medical Library, 8 Fenway, Boston, on Thursday, December 2, at 4:00 p.m.

POSTGRADUATE SEMINAR AT METROPOLITAN STATE HOSPITAL

A postgraduate seminar in neurology and psychiatry will be held at the Metropolitan State Hospital, Waltham, Massachusetts, during the coming fall and winter. The first semester, covering neurology, will consist of forty two-hour lectures each Friday from 10:00 a.m. to 9:00 p.m., beginning on October 1 and ending on December 10. The second semester, covering psychiatry, will consist of thirty-two two-hour lectures each Friday from 10:00 a.m. to 9:00 p.m., starting on March 3 and ending on April 24.

The seminar is open to all graduate physicians; it is sponsored by the Massachusetts Department of Mental Health, and there will be no charge. Those who are interested should communicate with Dr. William C. Gabler, Superintendent, Metropolitan State Hospital, Waltham.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 23

THURSDAY, SEPTEMBER 23

*10:30–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, SEPTEMBER 27

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, SEPTEMBER 28

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

2:00–4:00 p.m. Myasthenia gravis clinic. Out Patient Department, Massachusetts General Hospital.

WEDNESDAY, SEPTEMBER 29

*12:00 m. Clinicopathological conference. Children's Hospital.

4:00 p.m. Fiftieth Anniversary of Tufts College Medical School.

*Open to the medical profession.

SEPTEMBER 15–OCTOBER 6. Fiftieth Anniversary of Tufts College Medical School. Page xii, issue of September 9, and notice elsewhere on this page.

OCTOBER 6. Conference and Seminar in Legal Medicine. Page viii, issue of August 12.

(Notices continued on page xv)

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*A Simple Micromethod for the Detection of Acetone in Urine: Brem, J., *New Eng. J. Med.*, 224:462, 1941.

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October 11. Cancer Symposium. Page 493.

October 11–22. 1943 Graduate Fortnight of the New York Academy of Medicine. Page 32, issue of July 1.

October 14. Inhalation Therapy in Serious Respiratory Disease. Dr. Maurice S. Segal. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

October 21–23. Association of Military Surgeons of the United States. Page x, issue of September 2.

District Medical Society

SUFFOLK

December 2. Censors' meeting. Page x.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Essentials of Syphilology. By Rudolph H. Kampmeier, M.D., associate professor of medicine, Vanderbilt University School of Medicine, and in charge of the Syphilis Clinic and visiting physician, Vanderbilt University Hospital. With chapters by Alvin E. Keller, M.D., and J. Cyril Peterson, M.D. 8°, cloth, 518 pp., with 87 illustrations and 52 tables. Philadelphia: J. B. Lippincott Company, 1943. $5.00.

This is a new manual intended for the general practitioner; it is based on a number of years of postgraduate teaching of the subject. Space is not given to the technic or details of the various serologic tests, since the general practitioner deals only with the interpretation of results. Differential diagnosis is limited to conditions that are commonly encountered.

TUFTS MEDICAL SCHOOL

Postgraduate Courses for the General Practitioner

ELECTROCARDIOGRAPHY. September 27-October 1. To familiarize the general practitioner, through demonstrations and intensive study of records, with the present status of electrocardiogram interpretation. Dr. Heinz Magendantz in charge. Tuition fee $25.

INTERNAL MEDICINE. October 4-29. Mornings are devoted to staff conferences, ward rounds in the Joseph H. Pratt Diagnostic Hospital, and to examining patients in the different medical clinics of the Boston Dispensary. Afternoon lectures by physicians on their specialties. Dr. Samuel Proger in charge. Tuition fee $50.

ALLERGY. October 18-22. A course designed to familiarize the general practitioner wtih the present-day status of the diagnosis and treatment of allergic conditions. Lectures on hay fever, bronchial asthma, atopic eczema, urticaria, serum disease, histamine, and the pharmacology of allergic diseases. Clinic demonstrations at the Boston Dispensary. Course given by Dr. Ethan Allan Brown for minimum enrollment of six. Tuition fee $25.

PROCTOLOGY 1. October 25-30. Observation of operations, attendance at rectal and pruritus clinics of the Boston Dispensary and Cambridge Hospital, and illustrated lectures on the anatomy, physiology, pathology of the anus and rectum, and the diagnosis and treatment of anal, rectal, and colonic diseases. Dr. Edward T. Whitney in charge. Tuition fee $25.

Applications for admissions should be addressed to the

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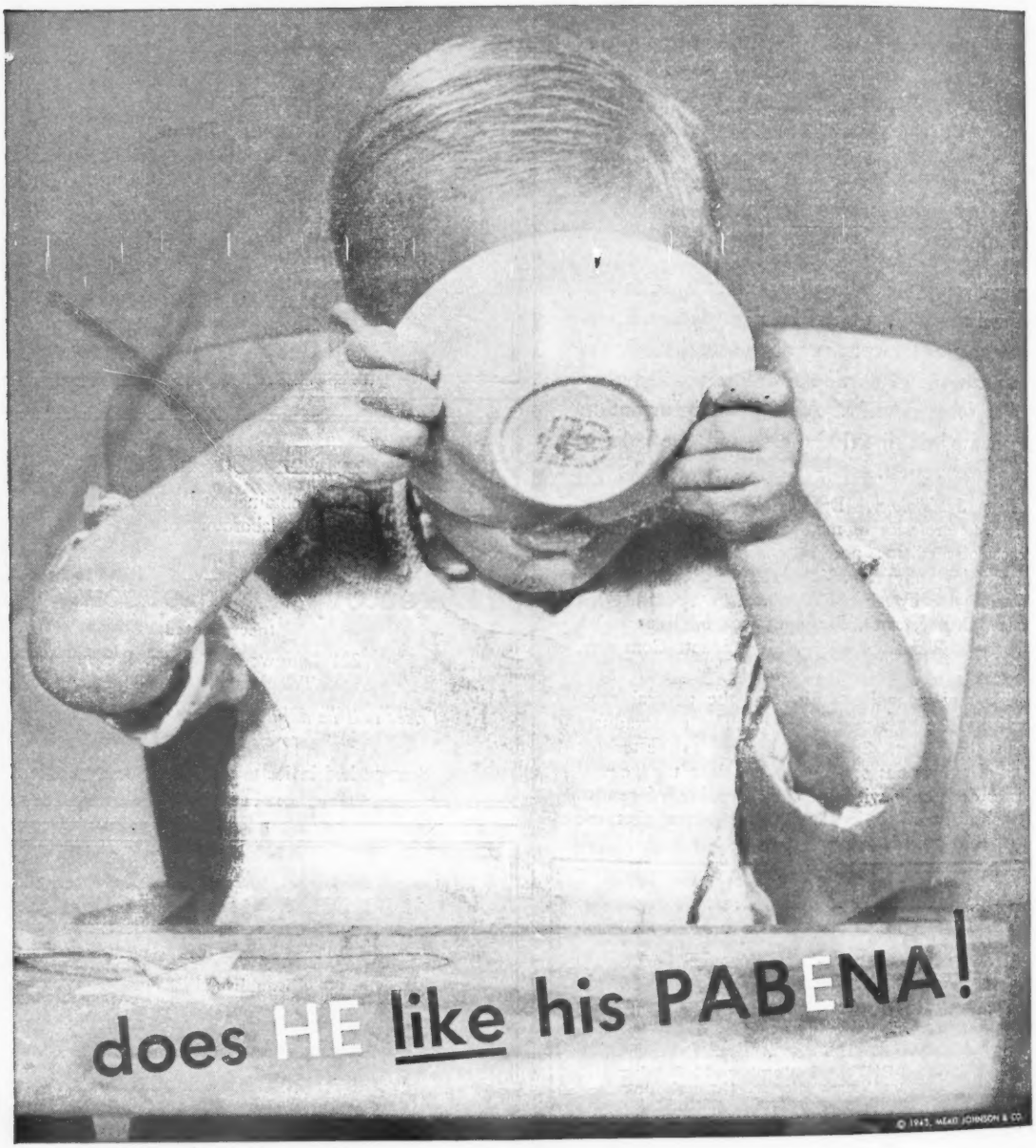

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